Connecting via Winsock to STN

* * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:05:33 ON 19 DEC 2006

=> file reaction

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FILE 'PS' ENTERED AT 10:05:55 ON 19 DEC 2006
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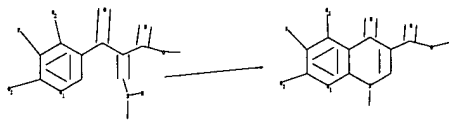
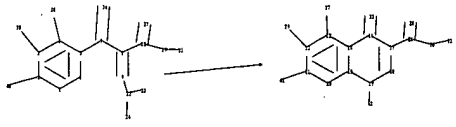
=>
Uploading C:\Program Files\Stnexp\Queries\10537945.str





chain nodes :
7 8 9 22 23 25 26 27 28 29 30 31 32 33 34 36 37 38 39 40 41
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19
ring/chain nodes :
24 42
chain bonds :
2-40 3-38 4-36 5-7 7-8 7-34 8-9 8-25 9-22 11-41 12-39 13-37 16-33
17-26 19-42 22-23 22-24 25-27 25-29 26-28 26-30 29-31 30-32

```
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  10-11  10-15  11-12  12-13  13-14  14-15  14-16
15-19  16-17  17-18  18-19
exact/norm bonds :
1-2  1-6  2-3  2-40  3-4  3-38  4-5  4-36  5-6  5-7  7-8  7-34  8-9  8-25  9-22
10-11  10-15  11-12  11-41  12-13  12-39  13-14  13-37  14-15  14-16  15-19  16-17
16-33  17-18  17-26  18-19  19-42  22-23  22-24  25-27  25-29  26-28  26-30  29-31
30-32


G1:C,N

G2:H,X

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom
22:CLASS  23:CLASS  24:CLASS  25:CLASS  26:CLASS  27:CLASS  28:CLASS  29:CLASS
30:CLASS  31:CLASS  32:CLASS  33:CLASS  34:CLASS  36:CLASS  37:CLASS  38:CLASS
39:CLASS  40:CLASS  41:CLASS  42:CLASS
fragments assigned product role:
containing 10
fragments assigned reactant/reagent role:
containing 1



L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=> s l1 full
FULL SEARCH INITIATED 10:06:47 FILE 'CASREACT'
SCREENING COMPLETE -      369 REACTIONS TO VERIFY FROM      106 DOCUMENTS

100.0% DONE     369 VERIFIED     207 HIT RXNS                     88 DOCS
SEARCH TIME: 00.00.01

FULL SEARCH INITIATED 10:06:49 FILE 'CHEMINFORMRX'
SCREENING COMPLETE -       41 REACTIONS TO VERIFY FROM       15 DOCUMENTS

100.0% DONE      41 VERIFIED      21 HIT RXNS                      9 DOCS
SEARCH TIME: 00.00.03

FULL SEARCH INITIATED 10:06:53 FILE 'DJSMONLINE'
SCREENING COMPLETE -        4 REACTIONS TO VERIFY FROM        4 DOCUMENTS

100.0% DONE       4 VERIFIED       4 HIT RXNS                       4 DOCS
SEARCH TIME: 00.00.02

FULL SEARCH INITIATED 10:06:56 FILE 'PS'
SCREENING COMPLETE -        4 REACTIONS TO VERIFY FROM        4 DOCUMENTS
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100.0% DONE 4 VERIFIED 3 HIT RXNS 3 DOCS
SEARCH TIME: 00.00.02

L3 104 L1

=> s l3 and potassium phosphate tribasic or (k3po4)
L4 283 L3 AND POTASSIUM PHOSPHATE TRIBASIC OR (K3PO4)

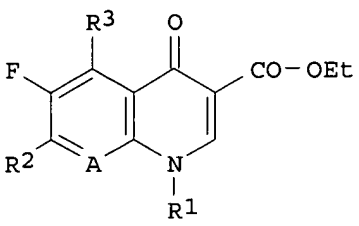
=> s l3 and((potassium phosphate tribasic) or (k3po4))
L5 1 L3 AND((POTASSIUM PHOSPHATE TRIBASIC) OR (K3PO4))

=> d ibib abs fhit

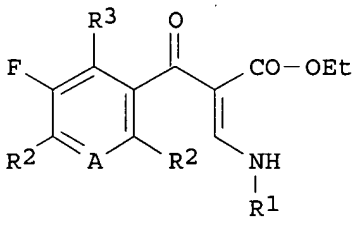
L5 ANSWER 1 OF 1 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 141:89022 CASREACT
TITLE: Preparation of quinolonecarboxylate derivatives
INVENTOR(S): Lee, Tai-Au; Park, Nam-Jin; Khoo, Ja-Heouk; Song, Seong-Ho; An, Ju-Young
PATENT ASSIGNEE(S): Yuhan Corporation, S. Korea
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056781	A1	20040708	WO 2003-KR2785	20031219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2004055527	A	20040626	KR 2002-82222	20021221
CA 2508341	A1	20040708	CA 2003-2508341	20031219
AU 2003286968	A1	20040714	AU 2003-286968	20031219
EP 1572657	A1	20050914	EP 2003-777472	20031219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006514033	T	20060427	JP 2004-562091	20031219
US 2006058528	A1	20060316	US 2005-537945	20050609
PRIORITY APPLN. INFO.:			KR 2002-82222	20021221
			WO 2003-KR2785	20031219

OTHER SOURCE(S): MARPAT 141:89022
GI



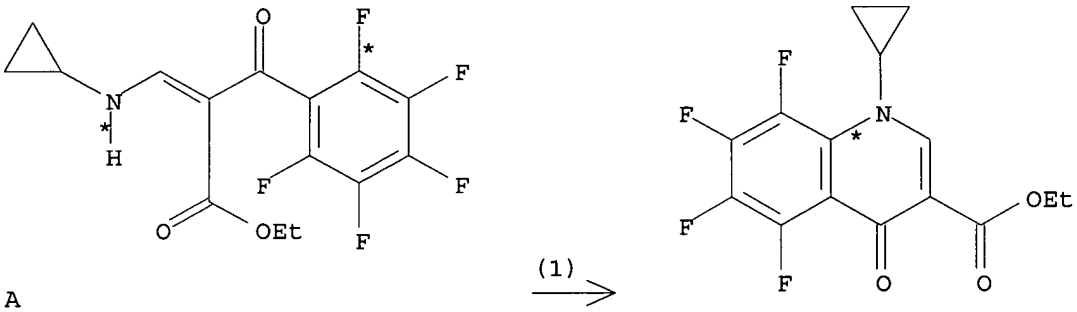
I



II

AB Title compds. I [R1 = cyclopropyl, 2,4-difluorophenyl, 1-acetoxy-2(S)-yl; R2, R3 = H, Cl, F; A = CH, CF, CNO2, N] are prepared by reaction of aminoacrylates II with K3PO4 in organic solvent. Thus, reaction of Et 3-cyclopropylamino-2-(pentafluorobenzoyl)acrylate in MeCN in the presence of K3PO4 at 75-80° for 1.5 h gave 96.9% Et 1-cyclopropyl-5,6,7,8-tetrfluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate.

RX(1) OF 7 A ===> B



A

B
YIELD 97%

RX(1) RCT A 107564-01-2
RGT C 7778-53-2 K3PO4
PRO B 107564-02-3
SOL 75-05-8 MeCN
CON 1.5 hours, 75 - 80 deg C
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

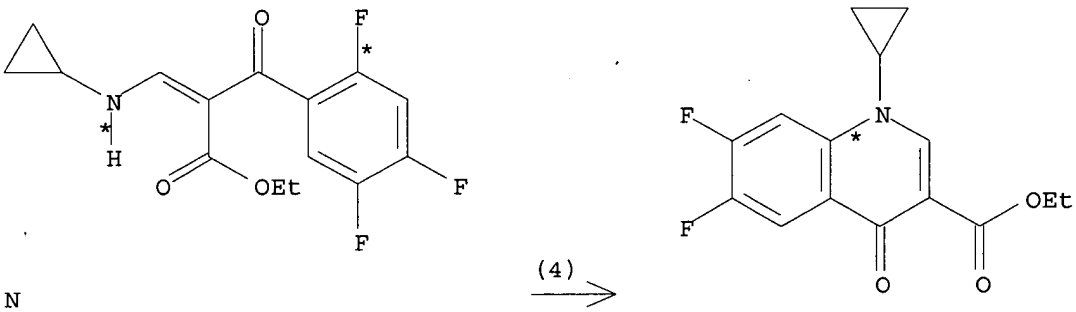
=ibib abs fhit

L7 ANSWER 1 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 145:8000 CASREACT
TITLE: Synthesis of a library of Ciprofloxacin analogues by means of sequential organic synthesis in microreactors
AUTHOR(S): Schwalbe, Thomas; Kadzimirsz, Daniel; Jas, Gerhard
CORPORATE SOURCE: CPC - Cellular Process Chemistry Systems GmbH, Mainz, D-55130, Germany
SOURCE: QSAR & Combinatorial Science (2005), 24(6), 758-768
CODEN: QCSSAU; ISSN: 1611-020X

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The realm of combinatorial chemical is strongly based on the concept of parallel chemical and its ease of automation. Although this batch-type approach in general may be considered a success story, some limitations remain rarely addressable by conventional approaches. Particularly, scaling-up problems such as the resynthesis of multi-gram amts. of active compds. as well as the synthesis of building blocks and scaffolds in large amts. may prove to be problematic. The authors' expertise in continuous chemical prompted them to develop a micro-reaction system for sequential organic synthesis that should overcome these limitations. In the present contribution a suitable system as well as its application to the first library approach towards (fluoro)quinolone antibiotics, such as Ciprofloxacin, solely using micro-reaction technol. is described. A known one-pot batch procedure for the synthesis of this compound class was split in its individual reaction steps, which were successfully adapted to a continuous conduct. After some optimization studies the overall sequence was suitable for chemical diversification. Particularly it was shown, that the first step of the synthesis - the acylation reaction of a β-dimethylamino acrylate with trifluoro-benzoic acid chloride - was accessible to synthesis of high quantities without any difficulties to yield a primary building block suitable for subsequent library synthesis. In a first diversification step, the Michael addition of a set of primary amines was followed by nucleophilic ring closure providing the difluoroquinolone system, which was subjected to a second diversification step by means of a nucleophilic aromatic substitution reaction. Thus, a number of Ciprofloxacin analogs could be synthesized in good overall yield and purity. Isolated yields ranged from 71 to 85% in the first diversification step and from 59 to 99% in the second step.

RX(4) OF 95 ...N ===> Q...



N

Q
YIELD 75%

RX(4) RCT N 101799-76-2
RGT R 6674-22-2 DBU
PRO Q 98349-25-8
SOL 872-50-4 NMEP
CON 120 deg C
NTE flow system used, key product, microreactor used, other base reagents could be also used, scalable

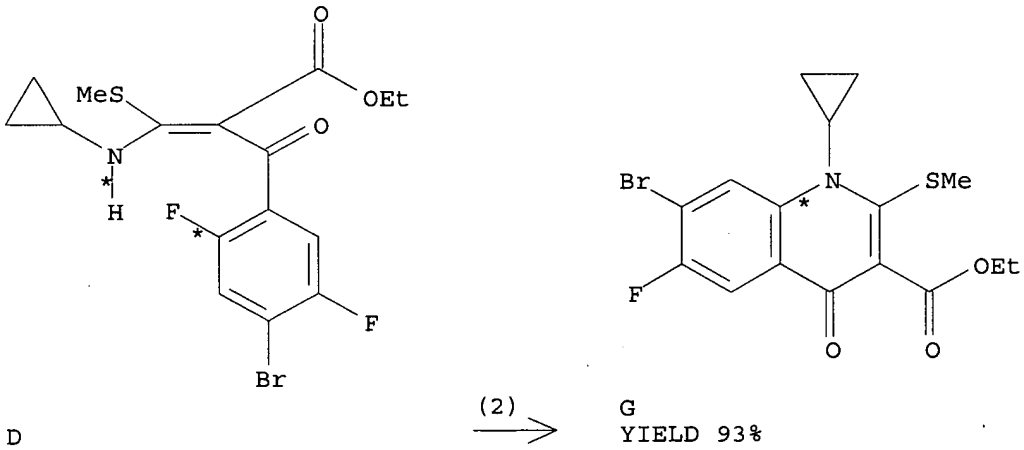
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 144:331317 CASREACT
TITLE: Isothiazoloquinolones containing functionalized aromatic hydrocarbons at the 7-position: Synthesis and in vitro activity of a series of potent antibacterial agents with diminished cytotoxicity in human cells
AUTHOR(S): Wiles, Jason A.; Wang, Qiuping; Lucien, Edlaine; Hashimoto, Akihiro; Song, Yongsheng; Cheng, Jijun; Marlor, Christopher W.; Ou, Yangsi; Podos, Steven D.; Thanassi, Jane A.; Thoma, Christy L.; Deshpande, Milind; Pucci, Michael J.; Bradbury, Barton J.
CORPORATE SOURCE: Achillion Pharmaceuticals, Inc., New Haven, CT, 06511-6653, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(5), 1272-1276
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This report describes 9H-isothiazolo[5,4-b]quinoline-3,4-diones (ITQs) containing aromatic groups at the 7-position that were prepared using palladium-catalyzed cross-coupling and tested against a panel of susceptible and resistant bacteria. In general, these compds. were more effective against Gram-pos. than Gram-neg. organisms. Many of the ITQs were more potent than contemporary quinolones and displayed a particularly strong antistaphylococcal activity against a clin. important, multi-drug-resistant strain. In contrast with ITQs reported previously, several of the analogs described in this Letter demonstrated low cytotoxic activity against a human cell line.

RX(2) OF 194 ...D ===> G...



D

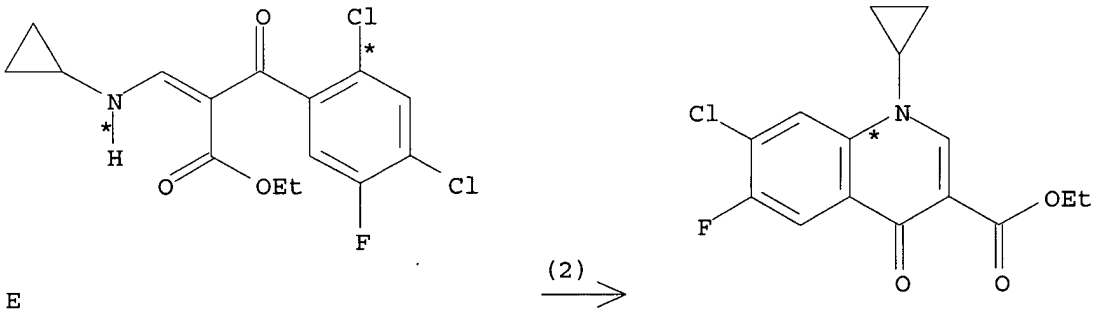
G
YIELD 93%

RX(2) RCT D 846563-92-6
RGT E 7646-69-7 NaH
PRO G 846563-93-7
SOL 68-12-2 DMF
CON 18 hours, 75 deg C

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 144:170865 CASREACT
TITLE: An expeditious synthesis of quinolone antibacterials
AUTHOR(S): Heravi, Majid M.; Oskooie, Hossein A.; Motamedi, Radineh; Ghassemzadeh, Mitra
CORPORATE SOURCE: Department of Chemistry, School of Sciences, Azzahra University, Tehran, Iran
SOURCE: Heterocyclic Communications (2005), 11(5), 423-426
CODEN: HCOMEX; ISSN: 0793-0283
PUBLISHER: Freund Publishing House Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A facile and rapid synthesis of ciprofloxacin under microwave irradiation is described. The product ciprofloxacin was isolated and the impurity was characterized as the product of substitution of F instead of Cl in 7-chloro-1-cyclopropyl-6-chloro-4(1H)-quinolone-3-carboxylic acid. Similarly norfloxacin was synthesized.

RX(2) OF 7 E ===> A...



E

A
YIELD 90%

RX(2) RCT E 86483-53-6
RGT C 497-19-8 Na2CO3
PRO A 86483-54-7
SOL 67-68-5 DMSO
CON 4 minutes
NTE microwave
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 143:405813 CASREACT
TITLE: Quinolone carboxylic acid derivatives for treatment of hyperproliferative conditions, their preparation and pharmaceutical compositions
INVENTOR(S): Khire, Uday; Liu, Xiao-Gao; Nagarathnam, Dhanapalan; Wood, Jill; Wang, Lei; Liu, Donglei; Zhao, Jin;

Guernon, Leatte; Zhang, Lei
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

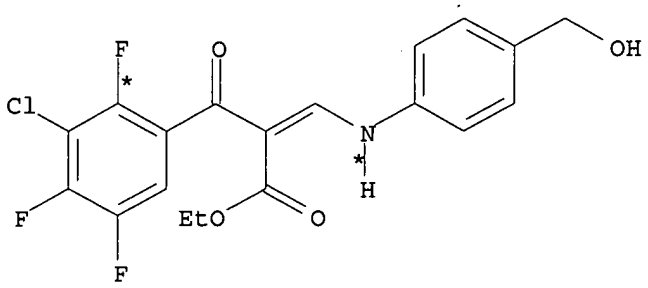
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005097752	A1	20051020	WO 2005-US10999	20050331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2561621	A1	20051020	CA 2005-2561621	20050331
PRIORITY APPLN. INFO.:			US 2004-558432P	20040331
			WO 2005-US10999	20050331

OTHER SOURCE(S): MARPAT 143:405813
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

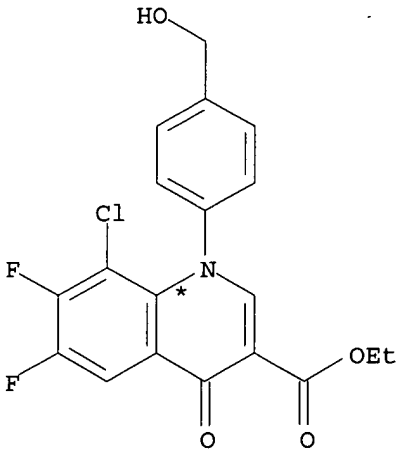
AB The invention relates to quinolone carboxylic acid derivs. of formula I. In compds. I, R1 is F, Cl, Br, NO2, (un)substituted C1-3 alkyl, or (un)substituted amino; R2 is F, Cl, Br, or optionally halo-substituted C1-3 alkyl; R3 is Cl, Br, optionally halo-substituted C1-3 alkyl, optionally halo-substituted C1-3 alkoxy, or cyano; R4 is mono- or disubstituted aminomethyl or aminoethyl; R5 is H, F, Cl, Br, optionally halo-substituted C1-3 alkyl, or optionally halo-substituted C1-3 alkoxy; R6 is NHR7 or OR7; R7 is selected from H and optionally halo-substituted C1-3 alkyl; Ar is (un)substituted Ph, (un)substituted pyridin-2-yl, or (un)substituted pyrimidin-2-yl; and Z is C or N. The invention also relates to the preparation of I, pharmaceutical compns. containing I and a pharmaceutically acceptable excipient, as well as to the use of the compns. for treating or preventing hyperproliferative disorders. Substitution of 4-nitrobenzyl bromide with pyrrolidine followed by hydrogenation gave 4-(pyrrolidin-1-ylmethyl)aniline, which condensed with Et 2-(3-chloro-2,4,5-trifluorobenzoyl)-3-ethoxyacrylate (II) to give quinolonecarboxylate III. III underwent regioselective substitution with 1-(2-pyridinyl)piperazine and ester hydrolysis resulting in the formation of quinolone-3-carboxylic acid IV. Most of the compds. of the invention, e.g., IV, express an IC50 value of less than 500 nM in an in vitro tumor cell proliferation assay.

RX(6) OF 387 ...AJ ===> AK...



AJ

(6) →



AK
YIELD 96%

RX(6) RCT AJ 866954-96-3
RGT J 584-08-7 K2CO3
PRO AK 866954-95-2
CAT 17455-13-9 18-Crown-6
SOL 109-99-9 THF
CON 40 minutes, room temperature
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

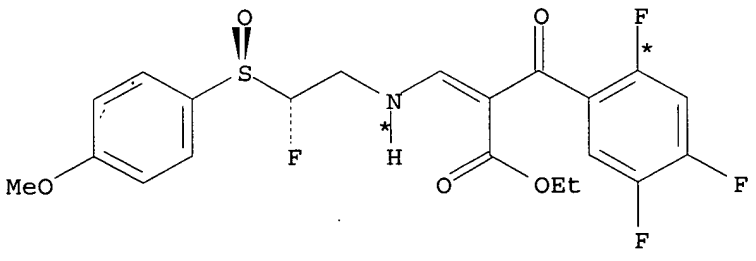
L7 ANSWER 5 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 143:7570 CASREACT
TITLE: Synthesis and Antibacterial Activity of 1-(2-Fluorovinyl)-7-substituted-4-quinolone-3-carboxylic Acid Derivatives, Conformationally Restricted Analogues of Fleroxacin
AUTHOR(S): Asahina, Yoshikazu; Iwase, Kazuhiko; Iinuma, Fujio; Hosaka, Masaki; Ishizaki, Takayoshi
CORPORATE SOURCE: Discovery Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Tochigi, 329-0114, Japan
SOURCE: Journal of Medicinal Chemistry (2005), 48(9),

3194-3202
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

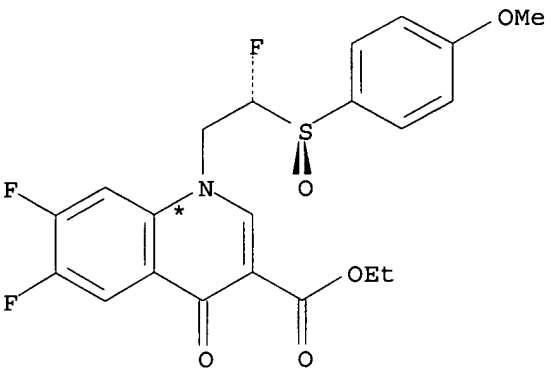
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Fluorovinyl oxoquinolinecarboxylic acids I (R = H, F; R1 = F, H; R2 = 4-methyl-1-piperazinyl, 3-amino-1-pyrrolidinyl; R3 = H, F, MeO), conformationally restricted analogs of fleroxacin II, are prepared and evaluated as DNA gyrase inhibitors for use as antibacterial agents. I are prepared using the (methoxyphenylsulfonyl)fluoroethylamine III as an intermediate; DAST-mediated fluorination of 2-(2-((4-methoxyphenyl)sulfonyl)ethyl)-1,3-isoindoledione, oxidation of the sulfide moiety generated in the first step with mCPBA, and hydrazine-mediated cleavage of the phthalimidyl moiety yields III along with a smaller amount of its diastereomer. Et 3-(2,4,5-trifluorophenyl)-3-oxopropanoates undergo condensation with DMF di-Me acetal and III followed by base-mediated cyclocondensation, thermal sulfoxide elimination, ester hydrolysis, and regioselective nucleophilic aromatic substitution with either 1-methylpiperazine or 3-(tert-butoxycarbonylamino)pyrrolidine (and acid-mediated Boc cleavage in the case of the pyrrolidine) to yield I or their monohydrochloride salts. The Z-isomers of I exhibit 2- to 32-fold more potent in vitro antibacterial activity than the corresponding E-isomers. I•HCl (R = F; R1 = H; R2 = 3-amino-1-pyrrolidinyl; R3 = F) is the most active of the compds. tested, inhibiting both Gram-pos. and Gram-neg. bacteria with MIC of < 1 μg/mL. The activity of I•HCl (R = H, F; R1 = F, H; R2 = 3-amino-1-pyrrolidinyl; R3 = F) against DNA gyrase is measured; while I (R = F; R1 = H; 3-amino-1-pyrrolidinyl; R3 = F) inhibits DNA gyrase with a similar IC50 value to II, I (R = H; R1 = F; R2 = 3-amino-1-pyrrolidinyl; R3 = F) is about three times less effective at inhibiting DNA gyrase than II. The energies of conformations of I (R = F; R1 = H; 3-amino-1-pyrrolidinyl; R3 = F) are determined by calcn. and compared to those of II.

RX(7) OF 161 ...Q ===> X...



Q (7) →



X
YIELD 77%

RX(7) RCT Q 852508-91-9
RGT Y 7646-69-7 NaH
PRO X 852508-94-2
SOL 109-99-9 THF
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 30 minutes
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

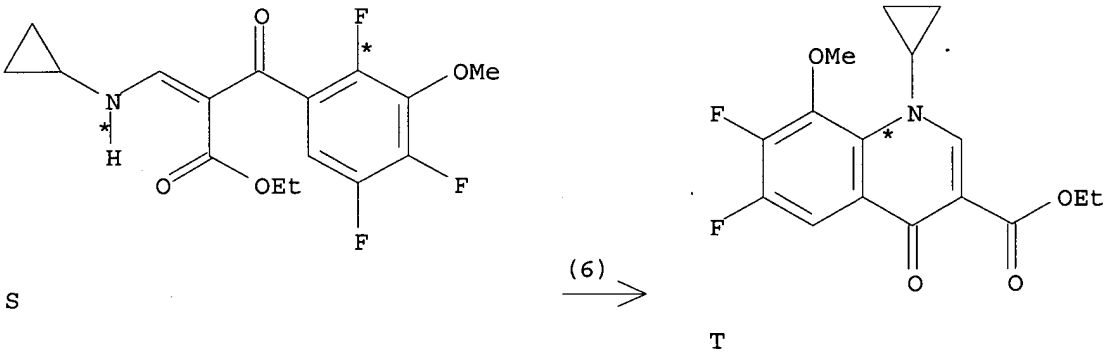
L7 ANSWER 6 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 142:430150 CASREACT
TITLE: Process for the preparation of gatifloxacin
INVENTOR(S): Xiao, Yunhua; Yong, Daoxin; Li, Liwei; Liang, Qun; Chang, Yan; Chen, Yulong; Lu, Xiaohong; Ye, Zhisong
PATENT ASSIGNEE(S): Baike Pharmaceutical Co., Ltd., Hubei, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1461748	A	20031217	CN 2002-115900	20020528

PRIORITY APPLN. INFO.: CN 2002-115900 20020528

AB A process for the preparation of gatifloxacin intermediate, Et 1-cyclopropyl-6,7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinolinecarboxylate (I), is disclosed. Chlorination of 2,4,5-trifluoro-3-methoxybenzoic acid with SOCl2 in anhydrous ethanol under refluxing gave 2,4,5-trifluoro-3-methoxybenzoyl chloride. Substitution of the acid chloride with di-Et malonate in toluene provided di-Et (2,4,5-trifluoro-2-methoxybenzoyl)malonate. Hydrolysis of this ester and addition of tri-Et orthoformate anhydride gave Et 3-ethoxy-2-(2,4,5-trifluoro-3-methoxybenzoyl)propenoate. Amination of this propenoate with cyclopropylamine and followed by cyclization gave the final product I.

RX(6) OF 21 ...S ===> T

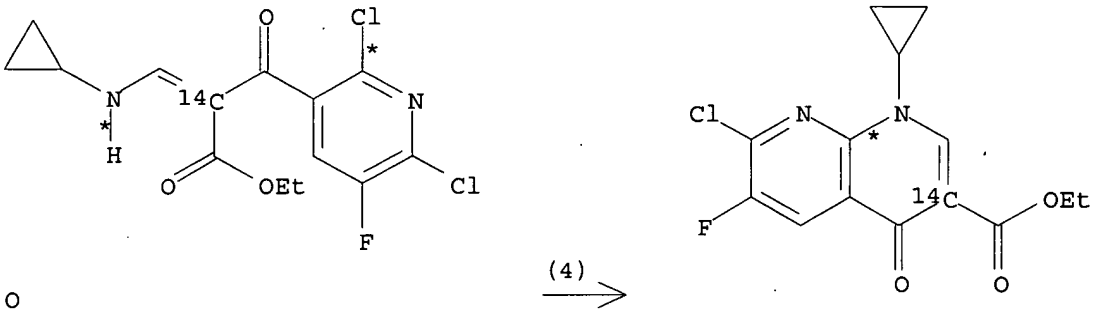


S T

RX(6) RCT S 112811-70-8
RGT U 497-19-8 Na2CO3
PRO T 112811-71-9
SOL 68-12-2 DMF
CON 1 hour, 100 deg C

L7 ANSWER 7 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 142:219455 CASREACT
TITLE: Synthesis of carbon-14 labeled gemifloxacin
AUTHOR(S): Shin, Hyun Il; Rim, Jong Gill; Lee, Ki Seung; Kim, Young Seok; Nam, Do Hyun; Shin, Hyun Ik; Chang, Jay Hyok; Oh, Chang Young; Ham, Won Hun
CORPORATE SOURCE: Korea RadioChemicals Center, Suwon, 440-745, S. Korea
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (2004), 47(11), 779-786
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new antibacterial agent gemifloxacin was labeled with carbon-14 for studies of pharmacokinetics and metabolism, the label was located in position 3 of the quinolone ring system. The overall radiochem. yield of the 14-step synthesis, starting from [2-14C]sodium acetate was 16.6%, and the radiochem. purity 97.5%.

RX(4) OF 36 ...O ===> S...



O

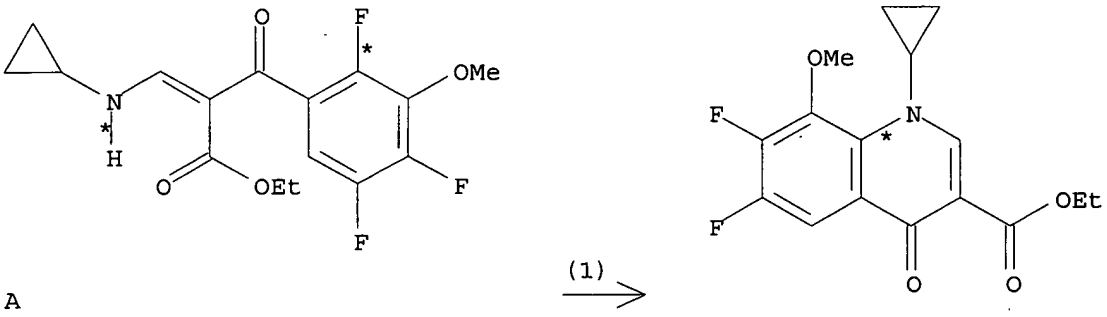
(4)

S
YIELD 83%

RX(4) RCT O 840475-02-7
RGT T 584-08-7 K2CO3
PRO S 840475-03-8
SOL 68-12-2 DMF
CON 2 hours, 90 deg C
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 142:134557 CASREACT
TITLE: Separation of the main impurity demethylgatifloxacin from gatifloxacin and its synthesis and identification
AUTHOR(S): Wang, Xiuzhen; Wang, Xintu; Wang, Erhua
CORPORATE SOURCE: Medicinal and Chemical Institute, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Zhongguo Yaoke Daxue Xuebao (2003), 34(3), 272-273
CODEN: ZHYXE9; ISSN: 1000-5048
PUBLISHER: Zhongguo Yaoke Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The main impurity of gatifloxacin was identified. Demethylgatifloxacin was synthesized in four steps from Et 2-(3-methoxy-2,4,5-trifluorobenzoyl)-3-(cyclopropylamino)acrylate through cyclization, chelation, N-piperazination, and hydrolysis, and identified by LC/MS, UV, 1HNMR, 13CNMR, MS.

RX(1) OF 6 A ===> B...



A

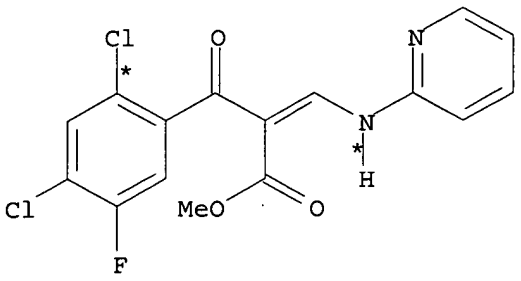
(1)

B
YIELD 85%

RX(1) RCT A 112811-70-8
RGT C 7789-23-3 KF
PRO B 112811-71-9
SOL 68-12-2 DMF
CON 5 hours, reflux

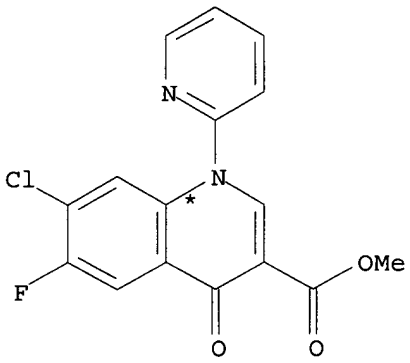
L7 ANSWER 9 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 141:106352 CASREACT
TITLE: Synthesis and antibacterial activity of N-pyridine quinolone derivative
AUTHOR(S): Wang, Dun-jia; Huang, Ling
CORPORATE SOURCE: Department of Chemistry and Environmental Engineering, Hubei Normal University, Huangshi, 435002, Peop. Rep. China
SOURCE: Huaxue Shiji (2004), 26(1), 47-49
CODEN: HUSHDR; ISSN: 0258-3283
PUBLISHER: Huagongbu Huaxue Shiji Xinsizhan
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB 1-(2-Pyridyl)-7-chloro-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)quinoline-3-carboxylic acid (I) was synthesized from 2,4-dichloro-5-fluoroacetophenone through β-keto-ester formation, condensation with tri-Et orthoformate, substitution with 2-aminopyridine, cyclization, chelation with boric acid in acetic anhydride and followed by nucleophilic substitution reaction with piperazine. The total yield was 39.3%. The in vitro antibacterial activity of I against S. aureus and E. coli was tested.

RX(3) OF 15 ...F ===> I...



F

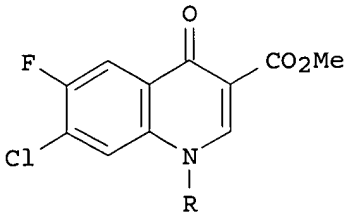
(3) →



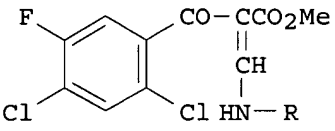
I
YIELD 93%

RX(3) RCT F 660852-20-0
RGT J 584-08-7 K2CO3
PRO I 660852-15-3
SOL 68-12-2 DMF
CON 2.5 hours, 125 - 130 deg C

L7 ANSWER 10 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:199182 CASREACT
TITLE: Study on the cyclization of antibacterial compounds quinolone derivatives
AUTHOR(S): Wang, Dun-jia; Fang, Zheng-dong
CORPORATE SOURCE: Dep. Chem. Environ. Eng., Hubei Normal Univ., Hubei Huangshi, 435002, Peop. Rep. China
SOURCE: Huaxue Fanying Gongcheng Yu Gongyi (2003), 19(3), 237-241
CODEN: HFGGEU; ISSN: 1001-7631
PUBLISHER: Zhejiangsheng Chuban Duiwai Maoyi Gongsi
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



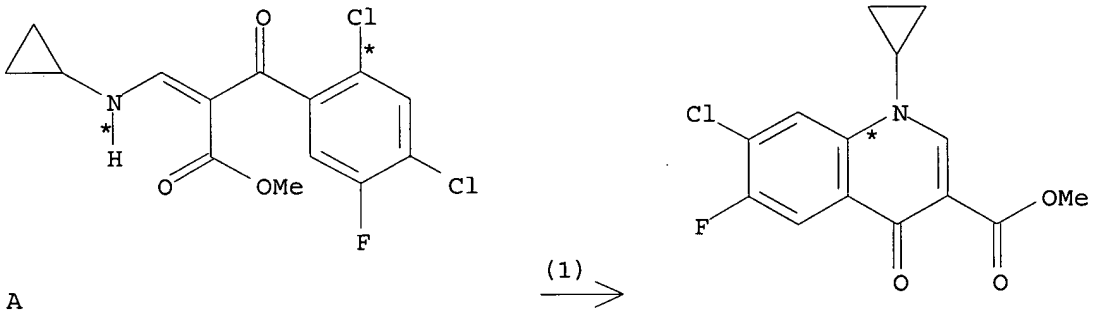
I



II

AB A series of N-substituted quinolone. derivs. I (R = cyclopropyl, Et, t-Bu, 2-pyridyl, 2-pyrimidyl, 2-thiazolyl) were prepared from II via an intramol. nucleophilic substitution reaction. The reaction conditions and intramol. nucleophilic substitution reaction activities were also investigated.

RX(1) OF 6 A ===> B



A

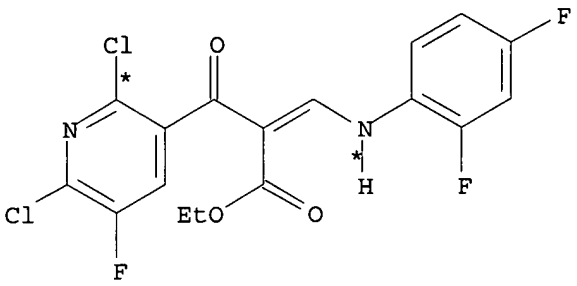
B
YIELD 91%

RX(1) RCT A 105392-26-5
RGT C 584-08-7 K2CO3
PRO B 104599-90-8
SOL 68-12-2 DMF
CON SUBSTAGE(1) room temperature -> 130 deg C
SUBSTAGE(2) 2.5 hours, 130 deg C
NTE optimization study

L7 ANSWER 11 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:28737 CASREACT
TITLE: Synthesis of tosufloxacin p-tosylate
AUTHOR(S): Liu, Mingliang; Sun, Lanying; Wei, Yonggang; Guo, Huiyuan
CORPORATE SOURCE: Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, 100050, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2003), 34(4), 157-158
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

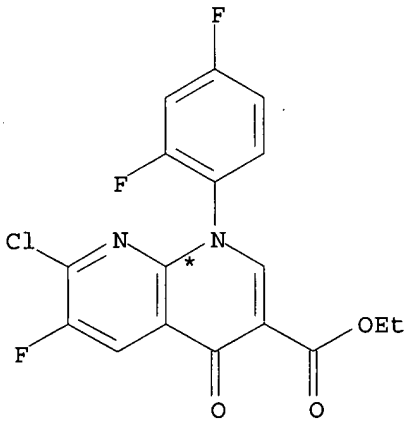
AB The title compound was prepared from Et 2,6-dichloro-5-fluoronicotinoylacetate via condensation with CH(OEt)3, 2,4-difluoroaniline displacement, cyclization, condensation with 3-aminopyrrolidine and hydrolysis in overall yield 72.6%.

RX(3) OF 21 ...F ===> H...



F

(3) →



H
YIELD 86%

RX(3) RCT F 100490-99-1

STAGE(1)
RGT I 584-08-7 K2CO3
SOL 109-99-9 THF
CON 3 hours, reflux

STAGE(2)
RGT J 7732-18-5 Water

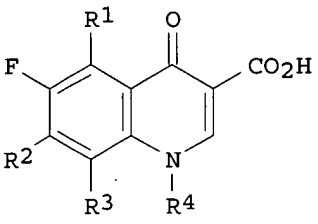
PRO H 100491-29-0

L7 ANSWER 12 OF 103 CASREACT COPYRIGHT 2006 ACS on STN

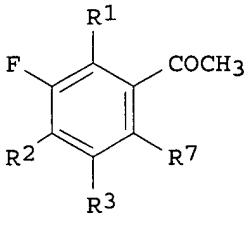
ACCESSION NUMBER: 138:287533 CASREACT
TITLE: Preparation of quinolonecarboxylic acids
INVENTOR(S): Wang, Yuncai; Chen, Rongye; Dong, Zhijun; Ben, Shijun; Nan, Haijun; Yu, Bingfan; Zhao, Chengwen
PATENT ASSIGNEE(S): Luyuan Industry Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 14 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1338455	A	20020306	CN 2000-123446	20000816
WO 2002059094	A1	20020801	WO 2001-CN1156	20010706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1319656	A1	20030618	EP 2001-980134	20010706
EP 1319656	B1	20060823		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517149	T	20040610	JP 2002-559396	20010706
AT 337304	T	20060915	AT 2001-980134	20010706
US 2003166936	A1	20030904	US 2003-344643	20030212
US 6699992	B2	20040302		
PRIORITY APPLN. INFO.:			CN 2000-123446	20000816
			WO 2001-CN1156	20010706

OTHER SOURCE(S): MARPAT 138:287533
GI



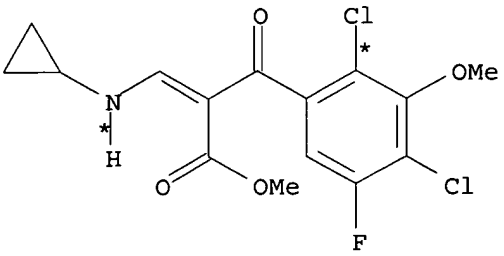
I



II

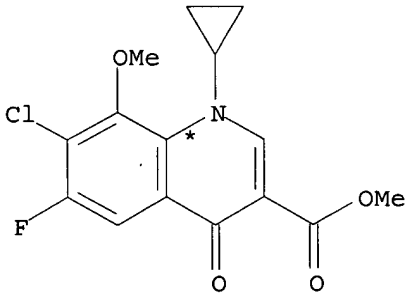
AB Title compds. I (R1 = H, halo, amino; R2 halo; R3 = H, halo, alkoxy, cyano; R4 = H, alkyl, cycloalkyl, alkoxy, alkoxyalkyl) are prepared from acetophenones II (R7 = halo) by condensing with carbonic acid ester, condensing with orthoformic acid ester and R4NH2, cyclizing in the presence of base, and then hydrolyzing.

RX(3) OF 62 ...G ===> J...



G

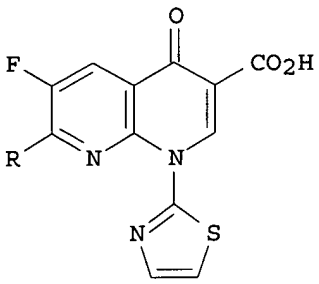
(3)



J
YIELD 90%

RX(3) RCT G 507266-00-4
RGT K 584-08-7 K2CO3
PRO J 507266-01-5
SOL 68-12-2 DMF
CON 2.5 hours, 40 - 45 deg C

L7 ANSWER 13 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 137:370056 CASREACT
TITLE: Synthesis and Structure-Activity Relationships of Novel 7-Substituted 1,4-Dihydro-4-oxo-1-(2-thiazolyl)-1,8-naphthyridine-3-carboxylic Acids as Antitumor Agents. Part 1
AUTHOR(S): Tomita, Kyoji; Tsuzuki, Yasunori; Shibamori, Koh-ichiro; Tashima, Masanori; Kajikawa, Fumie; Sato, Yuji; Kashimoto, Shigeki; Chiba, Katsumi; Hino, Katsuhiko
CORPORATE SOURCE: Chemistry Research Laboratories, Dainippon Pharmaceutical Co. Ltd., Osaka, 564-0053, Japan
SOURCE: Journal of Medicinal Chemistry (2002), 45(25), 5564-5575
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

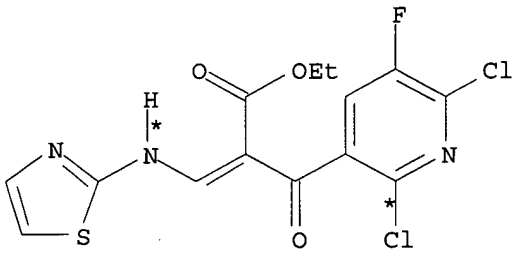


HCl

I

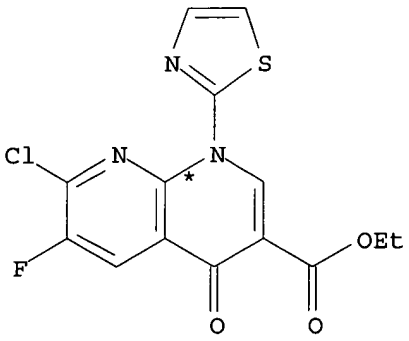
AB Title compds., e.g. I (R = H2NCH2CH2NH, 1-pyrrolidinyl, 3-hydroxy-1-pyrrolidinyl), possess moderate cytotoxic activity. Structure-activity relationships of title compds. were investigated by changing substituents at N-1 and C-7 positions and the core ring structure itself and evaluated the synthesized compds. against several murine and human tumor cell lines. The 2-thiazolyl group at the N-1 position of the naphthyridine structure is the best substituent for antitumor activity and regarding core ring structure, the naphthyridine derivative is the most active followed by pyridopyrimidine analog. At the C-7 position, aminopyrrolidine derivs. are more effective than other amines or thioether derivs. I (R = 3-amino-4-methoxy-1-pyrrolidinyl, 3-amino-3-methyl-1-pyrrolidinyl, 3-aminopyrrolidinyl) were determined to be effective in vitro and in vivo antitumor assays, and their activity was comparable to that of etoposide.

RX(2) OF 278 ...D ===> G...



D

(2) →

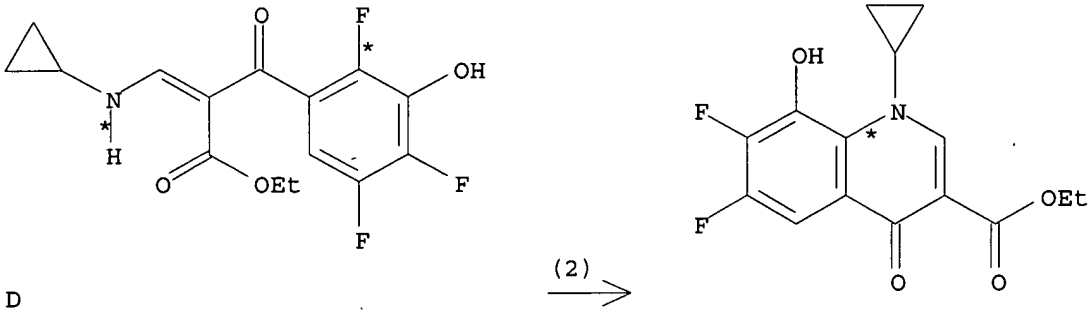


G
YIELD 63%

RX(2) RCT D 108118-70-3
RGT H 865-47-4 t-BuOK
PRO G 108118-77-0
SOL 123-91-1 Dioxane
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 137:201216 CASREACT
TITLE: New synthesis of Gatifloxacin
AUTHOR(S): Liu, Jiuyu; Tian, Zhiming; Guo, Huiyuan
CORPORATE SOURCE: Institute of Medicinal Biotechnology, Chinese Academy of medical Sciences and peking Union Medical College, Beijing, 100050, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2001), 32(10), 433-437
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Gatifloxacin was synthesized from 3-hydroxy-2,4,5-trifluorobenzoic acid via 13 steps, with low overall yield. Ten new compds. were obtained, and their structures were characterized by 1HNMR and MS.

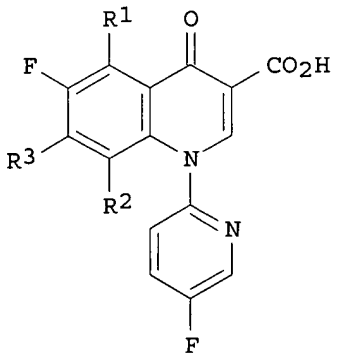
RX(2) OF 49 ...D ===> G...



D G
YIELD 36%

RX(2) RCT D 452092-29-4
RGT H 584-08-7 K2CO3
PRO G 452092-31-8
SOL 68-12-2 DMF

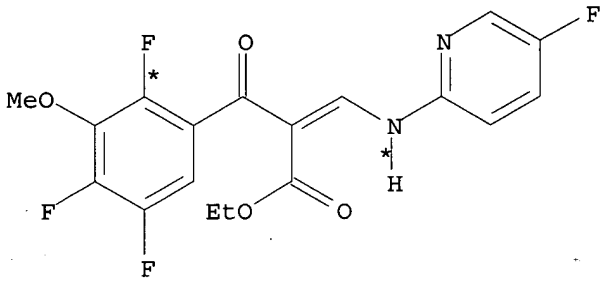
L7 ANSWER 15 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 136:325403 CASREACT
TITLE: Synthesis and antibacterial activity of 5-amino-6,8-difluoro- 1-(5-fluoro-2-pyridyl)-7-(3-methyl-1-piperazinyl)-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid and its analogues
AUTHOR(S): Liu, Jiuyu; Wei, Yonggang; Guo, Huiyuan
CORPORATE SOURCE: Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100050, Peop. Rep. China
SOURCE: Yaoxue Xuebao (2001), 36(6), 419-422
CODEN: YHHPAL; ISSN: 0513-4870
PUBLISHER: Yaoxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



I

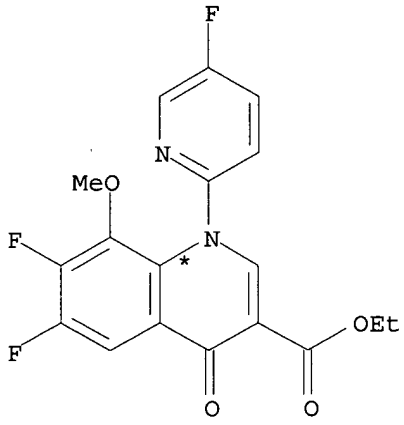
AB Title compds. I (R1 = H or amino; R2 = fluoro or 3-methyl-1-piperazinyl; and R3 = 3,5-dimethyl-1-piperazinyl, 4-methyl-1-piperazinyl; or 1-piperazinyl) were synthesized from Et 6-nitro-2,3,4,5-terafluorobenzoylacetate or Et 3-methoxy-2,4,5-trifluorobenzoylacetate by condensation with tri-Et orthoformate in the presence of acetic anhydride, substitution with 2-amino-4-fluoropyridine, cyclization in DMF in the presence of K2CO3, hydrolysis with HCl in acetic acid solution, and substitution with R3H in DMF or DMSO. Their structures were identified by 1HNMR and MS. The in-vitro antibacterial activities of the synthetic compds. against Staphylococcus aureus-16, Escherichia coli-26, and Pseudomonas aeruginosa-17 were lower than ciprofloxacin.

RX(4) OF 37 ...K ===> L...



K

(4) →



L
YIELD 84%

RX(4) RCT K 415714-13-5
RGT H 584-08-7 K2CO3
PRO L 415714-17-9
SOL 68-12-2 DMF

L7 ANSWER 16 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 136:279310 CASREACT

TITLE: Studies on pyridonecarboxylic acids as antibacterial agents XVI. Synthesis and antibacterial activity of 6-fluoro-1-(2-fluoro- 5-pyridinyl)-7-(1-piperazinyl)-1,4-dihydro-4-oxo-quinoline-3- carboxylic acid and analogues

AUTHOR(S): Qi, Jianjun; Guo, Huiyuan
CORPORATE SOURCE: Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100050, Peop. Rep. China

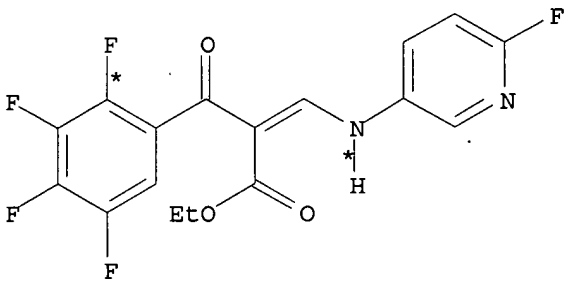
SOURCE: Zhongguo Kangshengsu Zazhi (2001), 26(2), 100-105
CODEN: ZKZAEY; ISSN: 1001-8689
PUBLISHER: Zhongguo Kangshengsu Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

GI

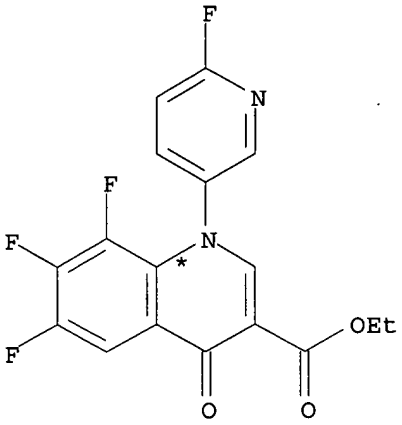
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I (R5 = H, NH2; R7 = 4-methylpiperazin-1-yl, 3-methylpiperazin-1-yl, 3,5- dimethylpiperazin-1-yl, piperazin-1-yl, 3-aminopyrrolidine-1-yl, 1,3-diaza-1-cyclooctyl, 1-pyrrolidinyl, 3-methylpiperid-1-yl; R8 = F, CH3O) were designed and synthesized from II (X1, X2 independently = F, Cl; R = CH3, CH3CH2; R5, R8 as above) by condensation reaction, cyclization, substitution reaction, and acid hydrolysis, etc. In vitro antibacterial activities of title compds. I were tested and compared with ciprofloxacin. The results showed title compds. I had only weak activity.

RX(1) OF 46 ...A ===> B...



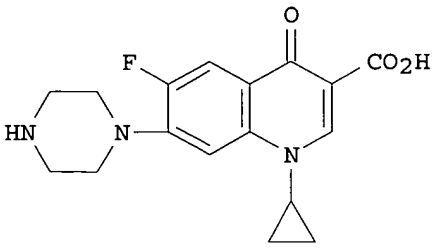
A (1) →



B
YIELD 80%

RX(1) RCT A 405555-80-8
RGT C 584-08-7 K2CO3
PRO B 405555-85-3
SOL 68-12-2 DMF
NTE 120°

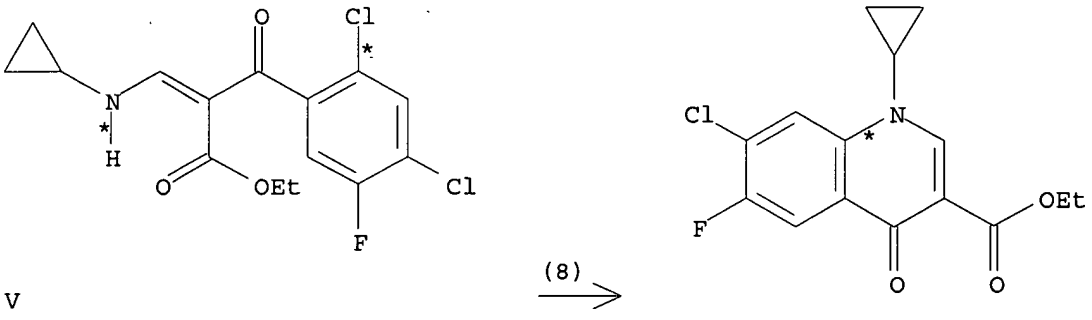
L7 ANSWER 17 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 136:183793 CASREACT
TITLE: In situ process for the synthesis of Ciprofloxacin
AUTHOR(S): Coll, Alberto Palomo; Morte, Sonia Serra
CORPORATE SOURCE: Centro Genesis para la Investigacion, Barcelona, 08021, Spain
SOURCE: Afinidad (2001), 58(494), 276-280
CODEN: AFINAE; ISSN: 0001-9704
PUBLISHER: Asociacion de Quimicos del Instituto Quimico de Sarria
DOCUMENT TYPE: Journal
LANGUAGE: Spanish
GI



I

AB Ciprofloxacin (I) is prepared in several steps starting from 3-chloro-4-fluoroaniline.

RX(8) OF 55 ...V ===> W...



V (8) W

RX(8) RCT V 86483-53-6

STAGE(1)
SOL 68-12-2 DMF

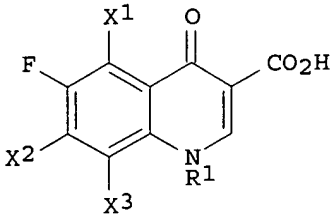
STAGE(2)
RGT X 584-08-7 K2CO3
CON 2 hours, 120 - 125 deg C

PRO W 86483-54-7
NTE key step
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 136:20088 CASREACT
TITLE: Process for the preparation of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxoquinolinecarboxylic acids in a cascade microreactor
INVENTOR(S): Schwalbe, Thomas; Taghavi-Moghadam, Shahriyar; Rueger, Reinhold
PATENT ASSIGNEE(S): CPC Cellular Process Chemistry G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1160241	A2	20011205	EP 2001-113350	20010601
EP 1160241	A3	20020814		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 10026903	A1	20020110	DE 2000-10026903	20000603

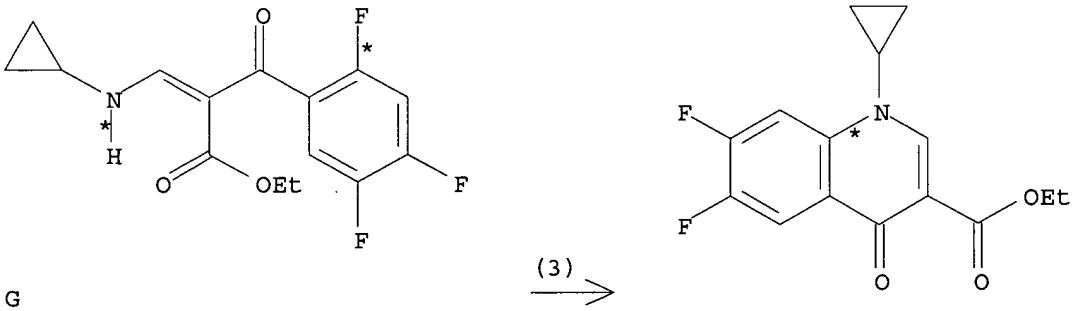
PRIORITY APPLN. INFO.: DE 2000-10026903 20000603
OTHER SOURCE(S): MARPAT 136:20088
GI



I

AB Title compds. [I; X1 = H, halo, alkyl, amino; X2 = halo, alkyl, (substituted) aryl, heteroaryl, ZR2, NR3; Z = O, S; R2, R3 = alkyl, (substituted) aryl, heteroaryl; R2R3 = heteroaryl; X3 = H, halo, alkyl, alkoxy, amino; R1 = alkyl, haloalkyl, cycloalkyl, (substituted) aryl, heteroaryl] are prepared by ≥1 continuous reaction of starting materials in a cascade microreactor. The starting materials in an inert solvent are mixed in a mixing zone and react in a reaction zone at elevated pressure and constant temperature I (1-cyclopropyl-6-fluoro-7-piperazin-1-yl-1,4-dihydro-4-oxoquinolinecarboxylic acid) was prepared in following steps (1) a mixture of Et dimethylaminoacrylate, Et3N, and MeCl3 and a mixture of 2,4,5-trifluorobenzoyl chloride, and MeCl3 were separated pumped in a microreactor followed by reaction at 60°, (2) the resulting Et 2-(2,4,5-trifluorobenzoyl)-3-dimethylaminoacrylate, glacial AcOH, and cyclopropylamine were mixed at 35° in another microreactor to give Et 2-(2,4,5-trifluorobenzoyl)-3-cyclopropylaminoacrylate, (3) the latter and N-methylpyrrolidone were mixed at 120° with a mixture of DBU and N-methylpyrrolidone followed by treatment with a mixture of piperazine, Et3N, t-BuOH, and N-methylpyrrolidone in a next microreactor to give 1-cyclopropyl-6-fluoro-7-piperazin-1-yl-1,4-dihydro-4-oxoquinolinecarboxylic acid Et ester, (4) the latter was saponified in a next microreactor to give 68% I.

RX(3) OF 15 ...G ===> I...



G

I

RX(3) RCT G 101799-76-2

STAGE(1)
SOL 872-50-4 NMEP

STAGE(2)
RGT J 6674-22-2 DBU

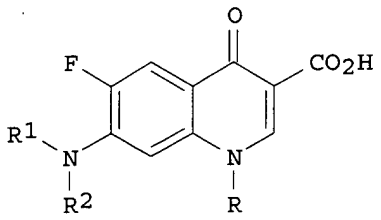
SOL 872-50-4 NMEP

PRO I 98349-25-8
NTE key step; microreactor

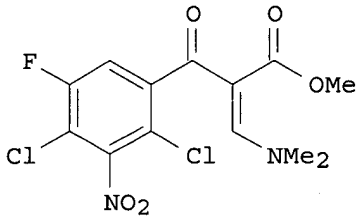
L7 ANSWER 19 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 135:371649 CASREACT
TITLE: An improved process for the preparation of quinolone derivatives, e.g. ciprofloxacin
INVENTOR(S): Pulla, Reddy Muddasani; Venkaiah, Chowdary Nannapaneni
PATENT ASSIGNEE(S): Natco Pharma Limited, India
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085692	A2	20011115	WO 2001-IN42	20010319
WO 2001085692	A3	20020606		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2415040	A1	20011115	CA 2001-2415040	20010319
AU 2001058718	A5	20011120	AU 2001-58718	20010319
EP 1282603	A2	20030212	EP 2001-932044	20010319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004073030	A1	20040415	US 2003-332759	20030228
PRIORITY APPLN. INFO.:			IN 2000-MA360	20000509
			WO 2001-IN42	20010319

OTHER SOURCE(S): MARPAT 135:371649
GI



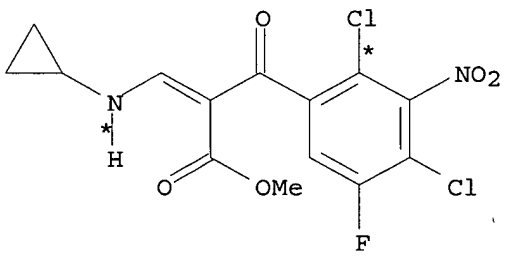
I



II

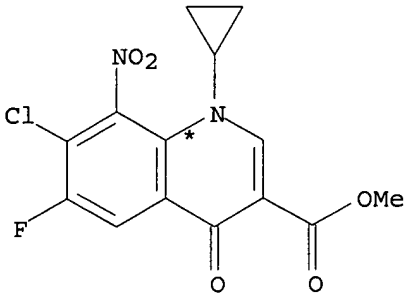
AB An improved process for the preparation of quinolone derivs. I [R = (cyclo)alkyl, aryl; R1-2 = diarylamino, arylalkylamino, dialkylamino, piperazinyl, morpholino, pyrrolidinyl, aralkyl, etc.] is disclosed. Et 3-dimethylaminoprop-2-enoate was reacted with 2,4-dichloro-5-fluoro-3-nitrobenzoyl chloride (PhMe, Et3N, reflux, 6 h) to give II. II was subjected to transamination with cyclopropylamine (MeOH, 0-10°C, 2-3 h) and cyclized (DMF, K2CO3, 60-70°C, 3 h) to give the corresponding N-cyclopropyl quinolone. This intermediate was reacted with piperazine (DMSO, NaHCO3), acetylated (CH2Cl2, Ac2O, room temperature) and the nitro group reduced (MeOH, Ra-Ni, H2, 20-30 psi, 3-4 h). The resulting aryl amine was deaminated (i. 10% aqueous H2SO4, NaNO2, 0°C, 15 min ii. 15% aqueous H3PO2, 25°C) and saponification (NaOH, 70-80°C, 3 h) to give ciprofloxacin (I, NR1R2 = piperazine; R = cyclopropyl) in 63% overall yield. The current process offers the following advantages over prior art: elimination of high temperature reactions, use of more efficient stoichiometry, more amenable to scale up and avoids impurities derived from fluoride displacement on the quinolone nucleus. I are useful as antibacterial drugs.

RX(3) OF 80 ...H ===> J...



H

(3)

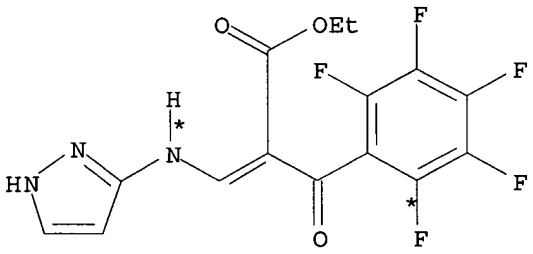


J

RX(3) RCT H 138998-54-6
RGT K 584-08-7 K2CO3
PRO J 104599-91-9
SOL 68-12-2 DMF

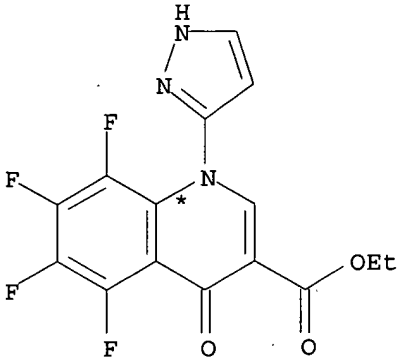
L7 ANSWER 20 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 135:344441 CASREACT
TITLE: Fluoro-containing heterocycles. V. Cyclization of 3-azolylamino-2-polyfluorobenzoylacrylates
AUTHOR(S): Lipunova, G. N.; Nosova, E. V.; Kodess, M. I.; Charushin, V. N.; Rozin, Yu. A.; Chasovskikh, O. M.
CORPORATE SOURCE: Ural State Technical University, Yekaterinburg, 620002, Russia
SOURCE: Russian Journal of Organic Chemistry (Translation of Zhurnal Organicheskoi Khimii) (2001), 37(4), 570-576
CODEN: RJOCEQ; ISSN: 1070-4280
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Heating Et 3-azolylamino-2-polyfluorobenzoylacrylates in acetonitrile in the presence of KF yielded derivs. of 1-azolyl-substituted quinolones or azolo[1,5-a]pyrimidines.

RX(2) OF 20 ...E ===> F



E

(2)

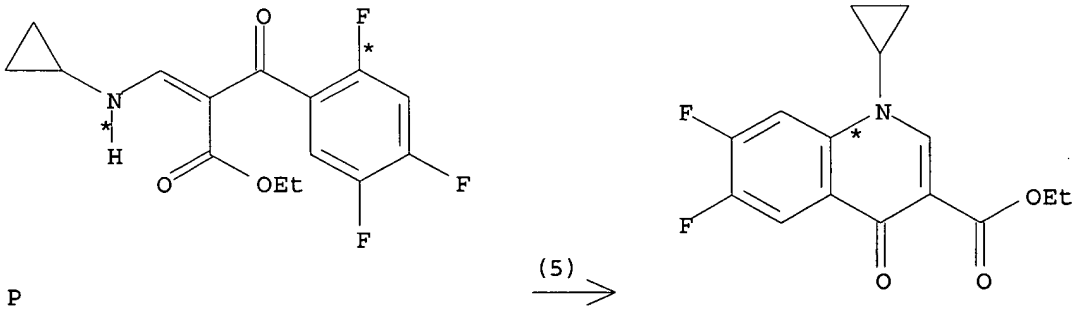


F
YIELD 70%

RX(2) RCT E 371249-07-9
RGT G 7789-23-3 KF
PRO F 371249-02-4
SOL 75-05-8 MeCN
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 134:115833 CASREACT
TITLE: Synthesis of clinafloxacin
AUTHOR(S): Huang, Shan; Li, Ze
CORPORATE SOURCE: Dept. of Physical Chemistry, China Pharmaceutical University, Nanjing, 210038, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2000), 31(8), 338-340
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The title bactericide was prepared in 8 steps in 21 % overall yield from 2,4,5-trifluorobenzoic acid.

RX(5) OF 45 ...P ===> Q...



P

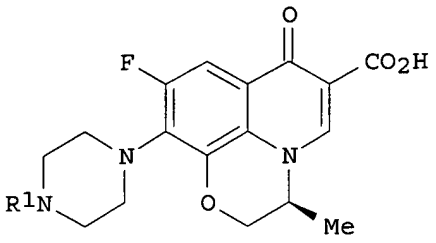
Q
YIELD 68%

RX(5) RCT P 101799-76-2
RGT R 584-08-7 K2CO3
PRO Q 98349-25-8
SOL 68-12-2 DMF

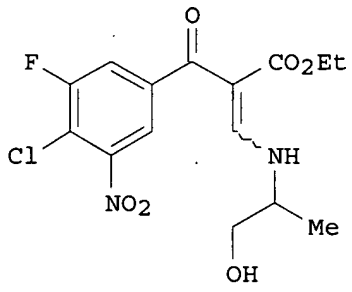
L7 ANSWER 22 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 133:193174 CASREACT
TITLE: Preparation of (-)-pyridobenzoxazinecarboxylates from (+)-ethyl 2-(4-chloro-5-fluoro-2-halo-3-nitobenzoyl)-3-[(1-hydroxypropy-2(S)-yl)amino]acrylate.
INVENTOR(S): Park, Young-jun; Lee, Ho-seong; Kim, Min-hwan; Kim, Kyung-chul
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050428	A1	20000831	WO 2000-KR145	20000223
W: BR, CN, IN, US				
RW: DE, ES, FR, GB, IT				
KR 2000056615	A	20000915	KR 1999-6093	19990224
JP 2000247980	A	20000912	JP 1999-228868	19990812
JP 3530784	B2	20040524		
BR 2000005132	A	20010102	BR 2000-5132	20000223
EP 1073662	A1	20010207	EP 2000-905443	20000223
EP 1073662	B1	20040414		
R: DE, ES, FR, GB, IT				
CN 1125073	B	20031022	CN 2000-800214	20000223
ES 2215024	T3	20041001	ES 2000-905443	20000223
JP 2000299412	A	20001024	JP 2000-47715	20000224
US 6316618	B1	20011113	US 2000-674323	20001024
PRIORITY APPLN. INFO.:			KR 1999-6093	19990224
			WO 2000-KR145	20000223

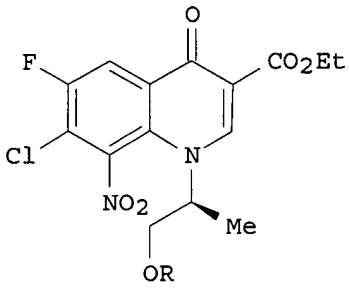
OTHER SOURCE(S): MARPAT 133:193174
GI



I



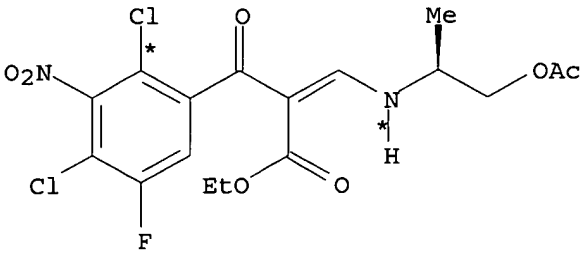
II



III

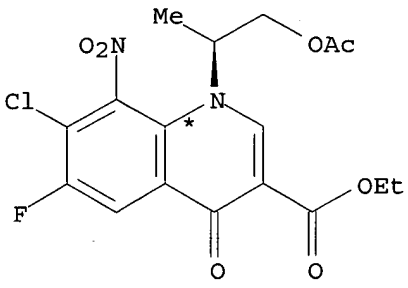
AB Title compds. (I; R1 = H, alkyl) were prepared by (1) reaction of aminoacrylates (II; X = halo; R = H) with RaZ [Ra = COR2; R2 = alkyl, alkoxy, cycloalkoxy, (substituted) Ph, etc.; Z = leaving group] or RbNCY [Rb = alkyl, (substituted) Ph] to give II [X = halo; R = COR2, RbNHCY; R2 = alkyl, alkoxy, cycloalkoxy, (substituted) Ph, etc.; Rb = alkyl, (substituted) Ph; Y = O, S], (2) treatment of the latter with base in an organic polar solvent to give III (R as above), (3) treatment of III with (R1-substituted) piperazine in an organic polar solvent in the presence of base, and (4) hydrolysis and cyclization in the presence of metal hydroxide in an organic solvent. Thus, (+)-Et 2-(2,4-dichloro-3-nitro-5-fluorobenzoyl)-3-[(1-hydroxyprop-2(S)-yl)amino]acrylate in ethylene dichloride at -40° was treated with Et3N and AcCl to give 100% (+)-Et 2-(2,4-dichloro-3-nitro-5-fluorobenzoyl)-3-[(1-acetoxypropyl-2(S)-yl)amino]acrylate. The latter was refluxed with K2CO3 in MeCN to give 96% (-)-Et N-(1-acetoxyprop-2(S)-yl)-6-fluoro-7-chloro-8-nitro-4-quinolone-3-carboxylate. This was refluxed with N-methylpiperazine and K2CO3 in MeCN to give 100% (-)-Et N-(1-acetoxyprop-2(S)-yl)-6-fluoro-7-(N-methylpiperazinyl)-8-nitro-4-quinolone-3-carboxylate. The latter was refluxed with KOH in EtOH to give 57% I (R1 = Me).

RX(1) OF 10 ...A ===> B...



A

(1) →



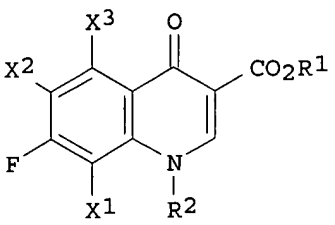
B
YIELD 96%

RX(1) RCT A 289688-76-2
RGT C 584-08-7 K2CO3
PRO B 289688-78-4
SOL 75-05-8 MeCN
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

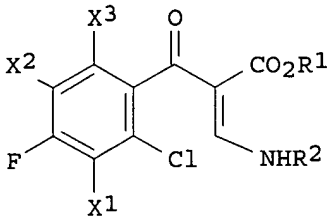
L7 ANSWER 23 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 131:31883 CASREACT
TITLE: Preparation of quinolinecarboxylic acid esters
INVENTOR(S): Hamada, Yusuke; Watanabe, Tsuneo; Umezu, Kazuto
PATENT ASSIGNEE(S): Ihara Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11147875	A	19990602	JP 1997-332397	19971117

PRIORITY APPLN. INFO.: JP 1997-332397 19971117
OTHER SOURCE(S): MARPAT 131:31883
GI



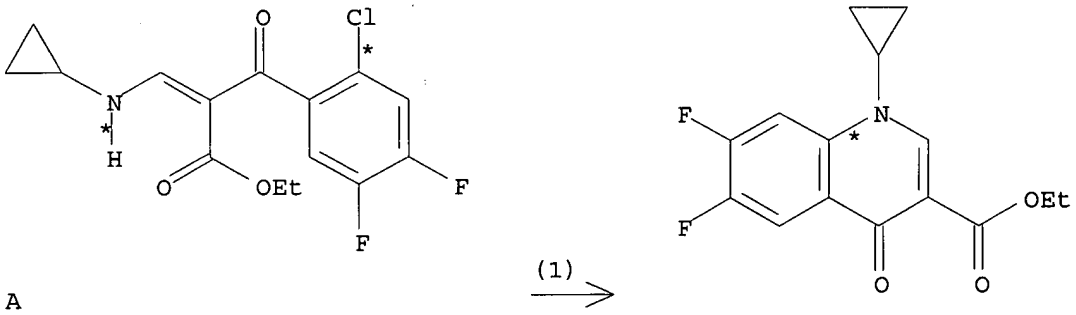
I



II

AB Title compds. I [R1 = C1-7 alkyl; R2 = (halo)cycloalkyl; X1 = H, F, Cl, C1-7 alkyl, C1-7 (halo)alkoxy; X2 = H, F, Cl; X3 = H, C1-7 alkyl, NO2] are prepared by cyclization of acrylic acid esters II (R1, R2, X1-X3 = same as I) with MnCO3 (M = alkali metal, alkaline earth metal; n = 1-2) in aprotic polar solvents. Et 3-cyclopropylamino-2-(2-chloro-4,5-difluorobenzoyl)acrylate was cyclized in DMF in the presence of K2CO3 at 120° for 4 h to give 93.0% Et 1-cyclopropyl-6,7-difluoro-4-oxoquinoline-3-carboxylate.

RX(1) OF 1 A ===> B



A

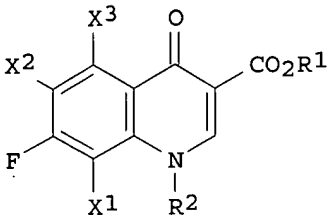
B
YIELD 93%

RX(1) RCT A 127371-49-7
RGT C 584-08-7 K2CO3
PRO B 98349-25-8
SOL 68-12-2 DMF

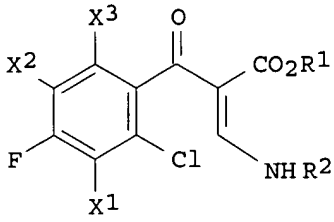
L7 ANSWER 24 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 128:34693 CASREACT
TITLE: Preparation of quinolinecarboxylic acid esters
INVENTOR(S): Watanabe, tsuneo; Umezu, Kazuto
PATENT ASSIGNEE(S): Ihara Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 09309880 A 19971202 JP 1996-127312 19960522
PRIORITY APPLN. INFO.: JP 1996-127312 19960522
OTHER SOURCE(S): MARPAT 128:34693
GI



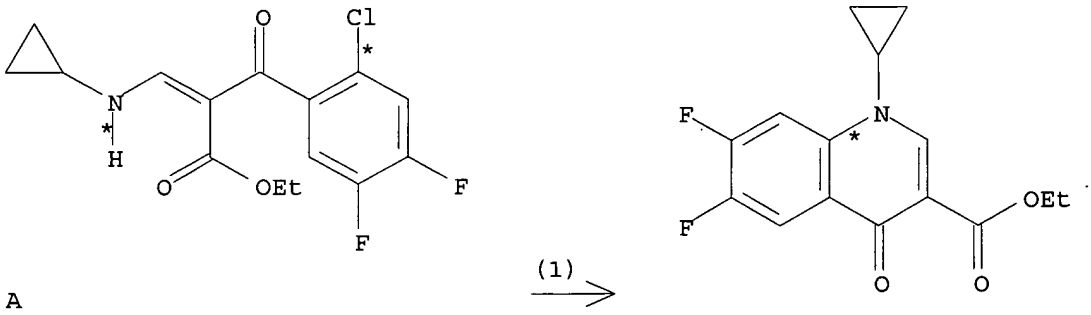
I



II

AB Title compds. I (R1 = C1-10 alkyl; R2 = (halo)cycloalkyl; X1 = H, F Cl, C1-10 alkyl, C1-10 alkoxy; X2 = H, F, Cl; X3 = H, alkyl, NO2) are prepared by cyclization of acrylic acid esters II (R1, R2, X1, X2, X3 = same as I) in R3CO2R4 (R3, R4 = C1-10 alkyl) as polar solvents using NaH as base. II (R1 = Et, R2 = cyclopropyl, X1 = X3 = H, X2 = F) (III) was treated with NaH in AcOEt at 60° for 4 h to give 96.6% I (R1, R2, X1, X2, X3 = same as III).

RX(1) OF 1 A ===> B



A

B
YIELD 96%

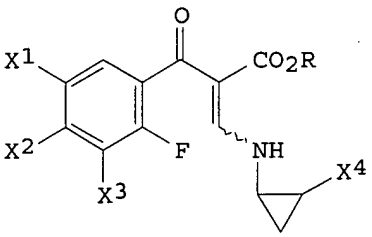
RX(1) RCT A 127371-49-7
RGT C 7646-69-7 NaH
PRO B 98349-25-8
SOL 141-78-6 AcOEt

L7 ANSWER 25 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 121:108555 CASREACT
TITLE: Preparation of quinolonecarboxylic acids as intermediates for microbicides
INVENTOR(S): Mikata, Ritsumasa; Shimizu, Sadahiro
PATENT ASSIGNEE(S): Daiichi Seiyaku Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent

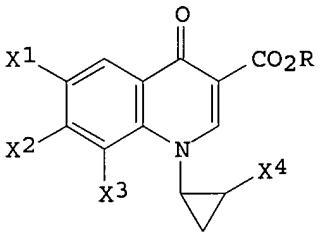
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06073013	A	19940315	JP 1992-227333	19920826
JP 3474593	B2	20031208		

PRIORITY APPLN. INFO.: JP 1992-227333 19920826
OTHER SOURCE(S): MARPAT 121:108555
GI



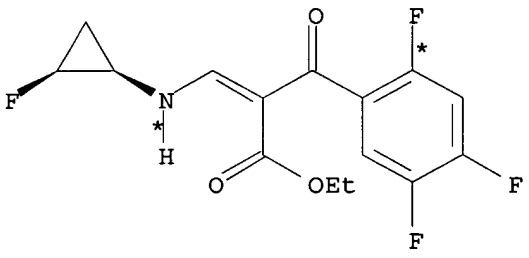
I



II

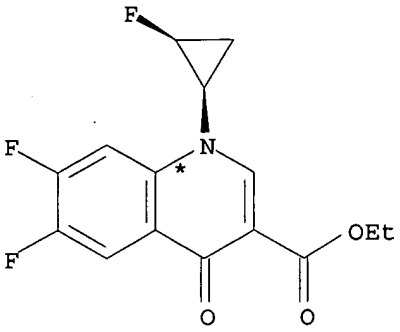
AB The title compds. II [R = lower alkyl, (lower alkyl-, lower alkoxy-, or halo-substituted) benzyl; X1-4 = H, halo], useful as intermediates for microbicides (no data), are prepared by treating amino(fluorobenzoyl)acrylates I (R, X1-4 = same as II) with bases and phase-transfer catalysts. A toluene solution of 1.5 g cis-I (R = Et, X1 = X2 = X4 = F, X3 = H) was treated with aqueous NaOH and Bu4NBr at room temperature for 4 h to give 1.39 g cis-II (R = Et, X1 = X2 = X4 = F, X3 = H).

RX(1) OF 1 A ===> B



A

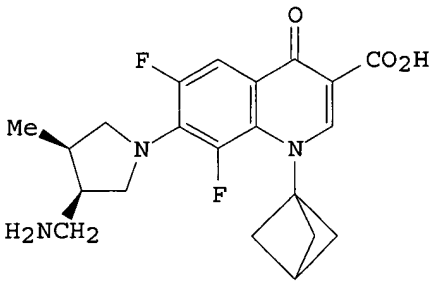
(1) →



B

RX(1) RCT A 151388-62-4
RGT C 1310-73-2 NaOH
PRO B 105919-22-0
CAT 1643-19-2 Bu4N.Br
SOL 7732-18-5 Water, 108-88-3 PhMe

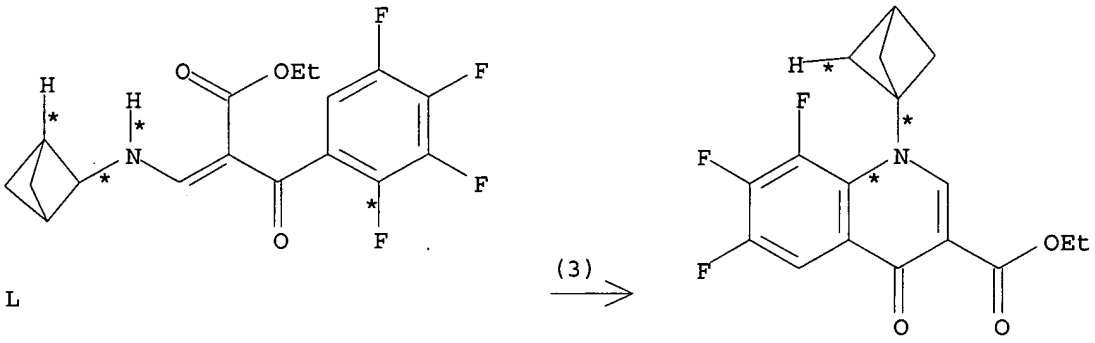
L7 ANSWER 26 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 120:54433 CASREACT
TITLE: U-87947E, a potent quinolone antibacterial agent incorporating a bicyclo[1.1.1]pent-1-yl (BCP) subunit
AUTHOR(S): Barbachyn, Michael R.; Hutchinson, Douglas K.; Toops, Dana S.; Reid, Raymond J.; Zurenko, Gary E.; Yagi, Betty H.; Schaadt, Ronda D.; Allison, John W.
CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1993), 3(4), 671-6
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Incorporation of a bicyclo[1.1.1]pent-1-yl group at the N-1 position of quinolone antibacterial agents affords compds. with potent activity. One of these analogs, I.MeSO3H (U-87947E), exhibits enhanced activity relative to that of ciprofloxacin against gram-pos. aerobic bacteria and anaerobic organisms. Time-kill kinetic studies reveal that U-87947E is exquisitely bactericidal against ciprofloxacin-resistant Staphylococcus aureus.

RX(3) OF 10 ...L ===> O...

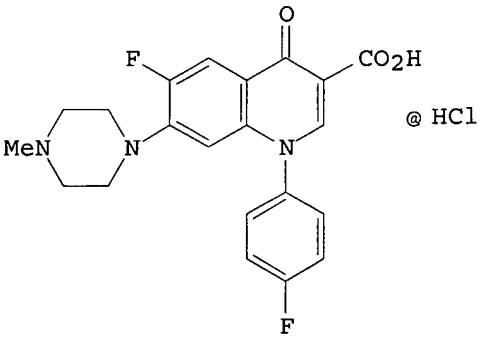


L

O

RX(3) RCT L 152253-32-2
RGT P 7646-69-7 NaH
PRO O 130682-30-3
SOL 109-99-9 THF

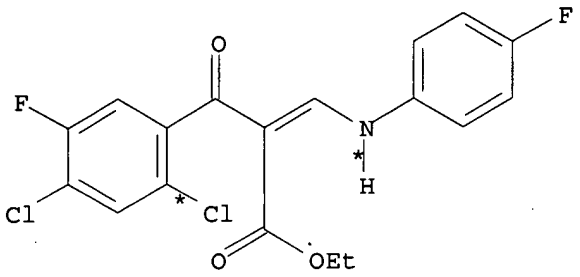
L7 ANSWER 27 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 119:117207 CASREACT
TITLE: Synthesis of difloxacin hydrochloride
AUTHOR(S): Guo, Huiyuan; Tian, Zhiming; Sun, Lanying; Cao, Yichen; Li, Zhuorong
CORPORATE SOURCE: Inst. Med. Biotechnol., Chin. Acad. Med. Sci., Beijing, 100050, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (1992), 23(12), 529-32
CODEN: ZYGZEA; ISSN: 1001-8255
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



I

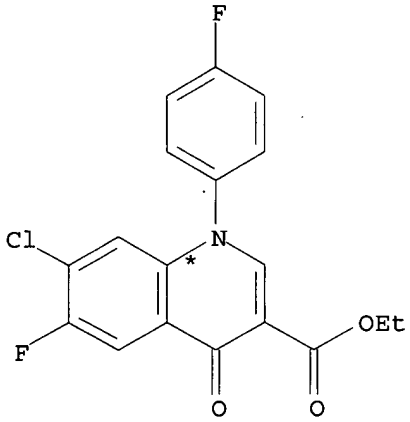
AB The title compound (I) was prepared in 8 steps starting from 2,4-dichlorofluorobenzene in 31.6% overall yield.

RX(3) OF 15 ...H ===> L...



H

(3)



L
YIELD 93%

RX(3) RCT H 98105-65-8
RGT M 584-08-7 K2CO3
PRO L 98105-80-7
SOL 68-12-2 DMF

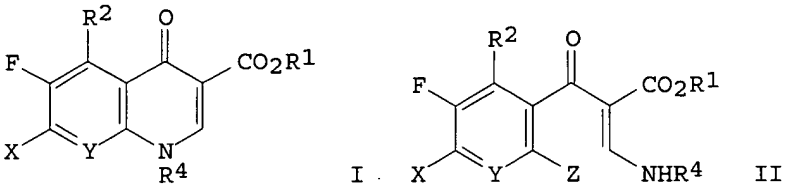
L7 ANSWER 28 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 119:95361 CASREACT
TITLE: Preparation of 4-oxoquinoline-3-carboxylic acids as bactericides
INVENTOR(S): Kamio, Chizuko; Oku, Masayoshi; Ataka, Kikuo
PATENT ASSIGNEE(S): Ube Industries, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

JP 05051365	A	19930302	JP 1991-324131	19911113
PRIORITY APPLN. INFO.:			JP 1991-103320	19910409

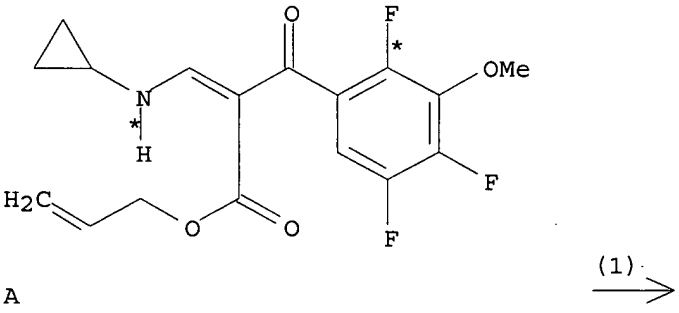
OTHER SOURCE(S): MARPAT 119:95361

GI

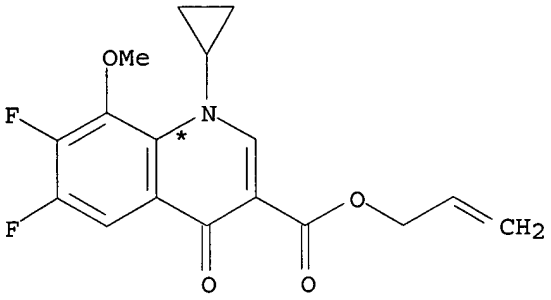


AB The title compds. I [R1 = C1-5 alkyl, alkenyl; R2 = H, F, NH2, NO2, PhCH2NH2; X = F, Cl; Y = N, CR3; R3 = H, halo, (fluorinated) MeO, lower alkyl, PhCH2O; R4 = (fluorinated) lower alkyl, cyclopropyl, fluoroinated Ph, N-formyl-N-methylamino, N-acetyl-N-methylamino], useful as bactericides (no data), are prepared by treatment of 3-alkylamino-2-benzoylacrylate esters II (R1, R2, R4, X, Y = same as above; Z = F, Cl) with Ti(OR)4 (R = lower alkyl, alkenyl). Treatment of 3.43 g allyl 3-dimethylamino-2-(2,4,5-trifluoro-3-methoxybenzoyl)acrylate (preparation given) with 0.62 g cyclopropylamine in THF at 50° for 2 h gave 3.5 g 3-cyclopropylamino-2-(2,4,5-trifluoro-3-methoxybenzoyl)acrylate, which (0.36 g) was refluxed with Ti(OCH2CH:CH2)4 in MePh to afford 87% I (R1 = allyl, R2 = H, R4 = cyclopropyl, X = F, Y = COMe) and 12% I (R1 = R2 = H, R4 = cyclopropyl, X = F, Y = COMe).

RX(1) OF 3 ...A ===> B



A



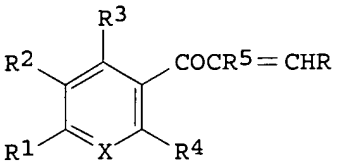
B
YIELD 87%

RX(1) RCT A 141290-13-3
RGT C 5128-21-2 2-Propen-1-ol, titanium(4+) salt
PRO B 141290-00-8
SOL 108-88-3 PhMe

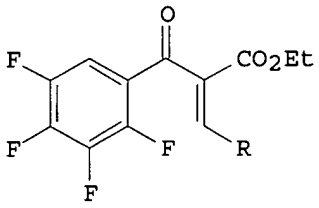
L7 ANSWER 29 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 117:48111 CASREACT
TITLE: Preparation of 3-amino-2-(het)aroylacrylic acid derivatives
INVENTOR(S): Grohe, Klaus
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 15 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4015299	A1	19911114	DE 1990-4015299	19900512
EP 457090	A2	19911121	EP 1991-106962	19910430
EP 457090	A3	19921125		
EP 457090	B1	19951129		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 130845	T	19951215	AT 1991-106962	19910430
ES 2082882	T3	19960401	ES 1991-106962	19910430
US 5182401	A	19930126	US 1991-694692	19910502
JP 07101918	A	19950418	JP 1991-131862	19910507
JP 2945507	B2	19990906		

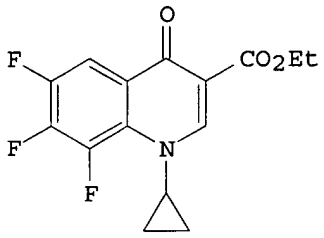
PRIORITY APPLN. INFO.: DE 1990-4015299 19900512
OTHER SOURCE(S): MARPAT 117:48111
GI



I



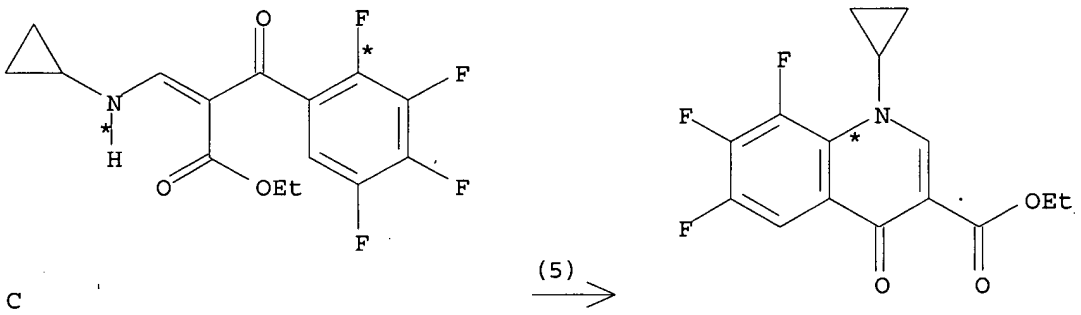
II



III

AB Amines I (R = NHR6; R1, R2 = halo; R3 = H, halo, NO2; R4 = halo, NO2, OMe, SMe; R5 = cyano, alkoxycarbonyl; R6 = alkyl, CH2CH2F, CH2CH2Cl, CH2CH2OH, CHMeCH2OH, cyclopropyl, OMe, 4-FC6H4, 2,4-F2C6H3, NMe2, NMeCHO, N:CMe2; X = N, CH, CMe, CNO2, COMe, CCN, halomethynyl) were prepared by transaminating I (R = dialkylamino). Thus, II (R = NMe2) was treated with cyclopropylamine in AcOH to give 98% II (R = cyclopropylamino) which was cyclized with NaF in N-methylpyrrolidone to give 90% quinolone III.

RX(5) OF 7 ...C ===> K



C

K
YIELD 90%

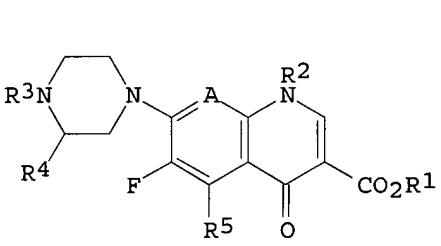
RX(5) RCT C 94695-51-9
RGT L 7681-49-4 NaF
PRO K 94242-51-0
SOL 872-50-4 NMEP

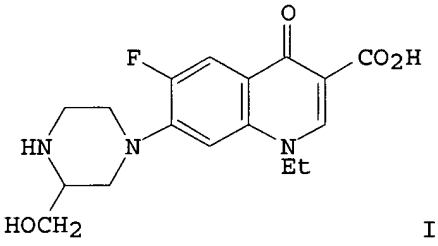
L7 ANSWER 30 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 114:228950 CASREACT
TITLE: Preparation of 7-(substituted)piperazinyl-1-ethyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acids as antibacterial agents

INVENTOR(S): Sum, Phaik Eng; Joseph, Joseph P.; Ziegler, Carl B., Jr.; Moran, Daniel B.; Lin, Yang I.
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: U.S., 33 pp. Cont.-in-part of U.S. Ser. No. 940,133, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4940710	A	19900710	US 1987-81786	19870805
US 5210193	A	19930511	US 1990-494386	19900316
PRIORITY APPLN. INFO.:			US 1986-820279	19860117
			US 1986-940133	19861217
			US 1987-81786	19870805

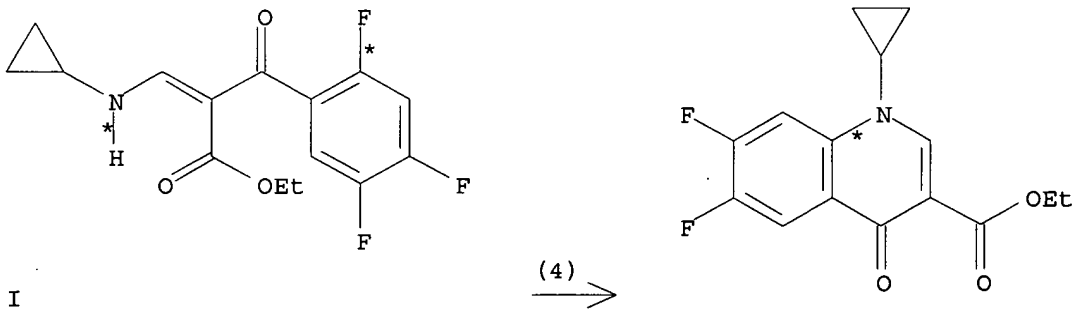
OTHER SOURCE(S): MARPAT 114:228950
GI


I


II

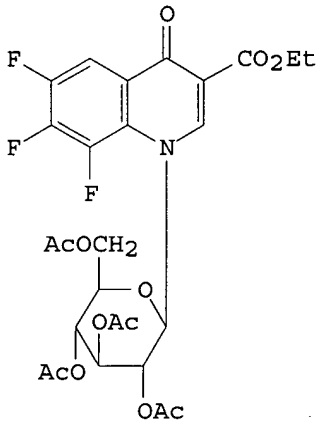
AB The title compds. I [R1 = H, alkyl, (dialkylamino)alkyl, N-piperidinoalkyl, etc.; R2 = alkyl, cycloalkyl, alkoxy, etc.; R3 = H, PhCH2, alkyl; R4 = fluoromethyl, difluoromethyl, cyclopropyl, etc.; R5 = H, F; A = N, CH, CF] were prepared A mixture of 2-(hydroxymethyl)piperazine and 7-chloro-1-ethyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid in pyridine was heated at 130° overnight to give, after workup and treatment with HCl, quinolone II.HCl. II.HCl in vitro exhibited MIC of 2 μg/mL against Escherichia coli ATCC 25922.

RX(4) OF 88 ...I ===> G...


I (4) G

RX(4) RCT I 101799-76-2
PRO G 98349-25-8
CAT 584-08-7 K2CO3

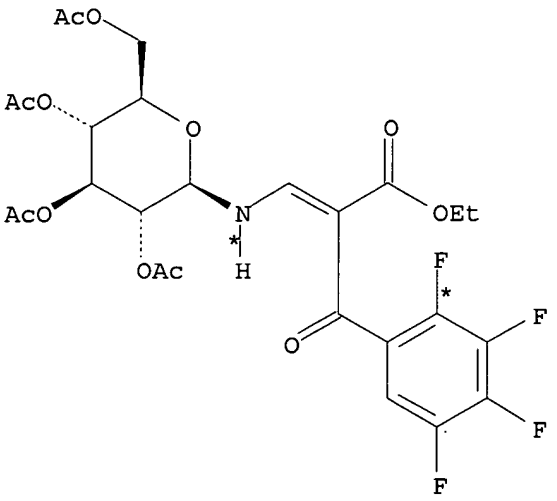
L7 ANSWER 31 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 114:185913 CASREACT
TITLE: Synthesis of a valuable precursor for the preparation of novel quinolone glycosides
AUTHOR(S): De la Cruz, Angeles; Elguero, Jose; Martinez, Ana
CORPORATE SOURCE: Inst. Quim. Med., CSIC, Madrid, E-28006, Spain
SOURCE: Synlett (1990), (12), 753-4
CODEN: SYNLES; ISSN: 0936-5214
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

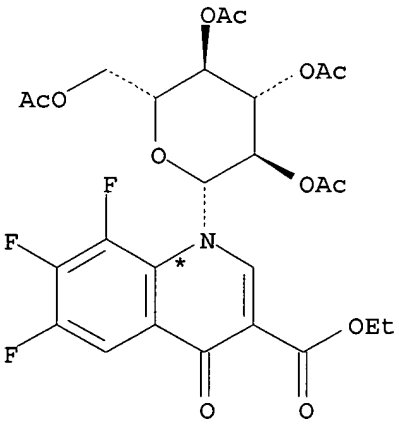
AB The synthesis of glycopyranosylethoxycarbonyltrifluoroquinolone I, a valuable key intermediate for the preparation of novel quinolone nucleosides, from the reaction of Et 2-ethoxymethylene-3-oxo-3-(2,3,4,5-tetrafluorophenyl)propanoate and 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylamine, is described.

RX(2) OF 5 ...C ===> F



C

(2) →



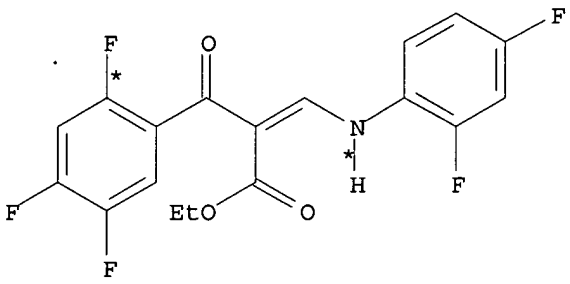
F
YIELD 68%

RX(2) RCT C 133491-09-5
RGT G 7646-69-7 NaH
PRO F 133491-11-9
SOL 109-99-9 THF
NTE KEY STEP; OTHER REACTANT ISOMER ALSO PRESENT

L7 ANSWER 32 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 114:42732 CASREACT
TITLE: Synthesis, antibacterial activities, and pharmacological properties of enantiomers of temafloxacin hydrochloride
AUTHOR(S): Chu, Daniel T. W.; Nordeen, Carl W.; Hardy, Dwight J.; Swanson, Robert N.; Giardina, William J.; Pernet,

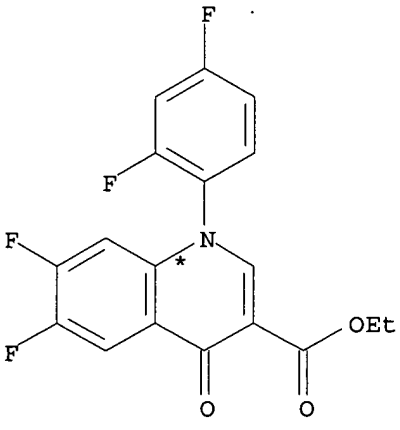
Andre G.; Plattner, Jacob J.
CORPORATE SOURCE: Anti-Infect. Res. Div., Abbott Lab., Abbott Park, IL, 66064-3500, USA
SOURCE: Journal of Medicinal Chemistry (1991), 34(1), 168-74
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Temafloxacin hydrochloride I is a potent member of the 4-pyridone-3-carboxylic acid class of antibacterial agents and is currently under clin. development as a broad-spectrum antimicrobial agent. It is a racemate having a chiral center at the C-3 of the 7-piperazin-1-yl group. The two enantiomers of I were synthesized and tested for their antibacterial activities. Although no difference of in vitro antibacterial activities was observed, a minor difference of in vivo antibacterial activities was observed However, they both exhibited similar pharmacol. profiles.

RX(4) OF 28 ...O ===> R...



O

(4)

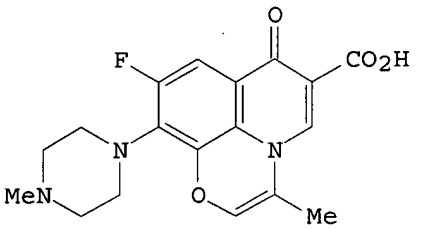


R
YIELD 77%

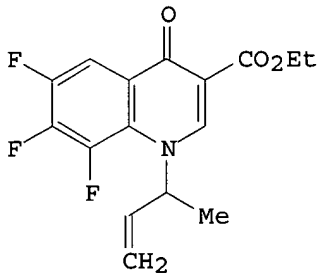
RX(4) RCT O 108115-67-9
RGT S 7646-69-7 NaH

PRO R 108138-17-6
SOL 109-99-9 THF

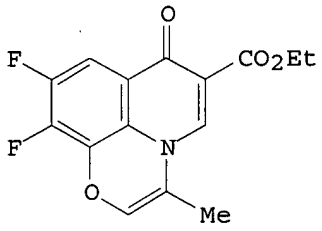
L7 ANSWER 33 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 113:231325 CASREACT
TITLE: Synthesis and antibacterial activity of 2,3-dehydroofloxacin
AUTHOR(S): Augeri, David J.; Fray, Andrew H.; Kleinman, Edward F.
CORPORATE SOURCE: Pfizer Cent. Res., Groton, CT, 06340, USA
SOURCE: Journal of Heterocyclic Chemistry (1990), 27(5), 1509-11
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



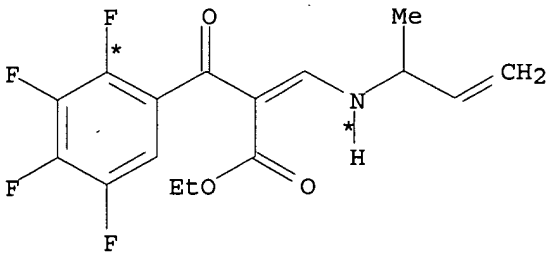
II



III

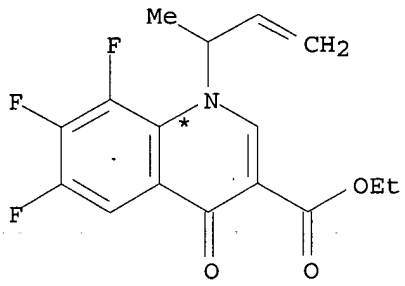
AB The 2,3-dehydro analog I of the potent quinolone antibacterial agent ofloxacin was synthesized by an efficient six step route beginning with Et 2,3,4,5-tetrafluorobenzoylacetate. Formation of oxazine ring of I was accomplished by ozonolysis of the 1-(1-buten-3-yl)quinolone II to the corresponding aldehyde, which cyclized upon treatment with base via intramol. displacement of the C-8 fluorine to afford tricyclic ester III. The antibacterial activities of 2,3-dehydroofloxacin and ofloxacin are compared.

RX(2) OF 15 ...D ===> G...



D

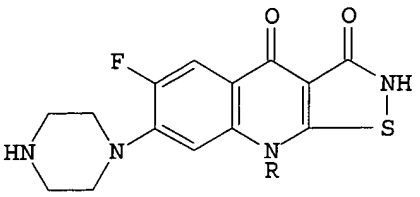
(2) →



G
YIELD 95%

RX(2) RCT D 130713-34-7
RGT H 7646-69-7 NaH
PRO G 130713-35-8
SOL 110-71-4 (CH2OMe)2

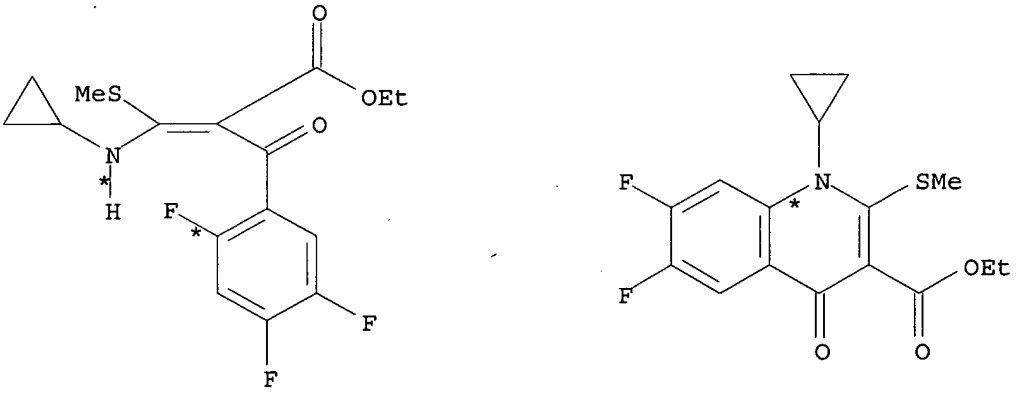
L7 ANSWER 34 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 113:152298 CASREACT
TITLE: Syntheses of 6-fluoro-7-piperazin-1-yl-9-cyclopropyl-2,3,4,9-tetrahydroisothiazolo[5,4-b]quinoline-3,4-dione and 6-fluoro-7-piperazin-1-yl-9-(p-fluorophenyl)-2,3,4,9-tetrahydroisothiazolo[5,4-b]quinoline-3,4-dione
AUTHOR(S): Chu, Daniel T. W.
CORPORATE SOURCE: Anti-infective Res. Div., Abbott Lab., Abbott Park, IL, 60064-3500, USA
SOURCE: Journal of Heterocyclic Chemistry (1990), 27(4), 839-43
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The syntheses of 6-fluoro-7-piperazin-1-yl-2,3,4,9-tetrahydroisothiazolo[5,4-b]quinoline-3,4-diones I (R = cyclopropyl, p-FC6H4) as well as a novel synthesis of isothiazolo-3(2H)-one system are described. Key steps include the regiospecific displacement of a sulfinyl group and the amination of the resulting mercapto derivative followed by an intramol. nucleophilic displacement cyclization reaction to generate the novel 2,3,4,9-tetrahydroisothiazolo[5,4-b]quinoline-3,4-dione nucleus.

RX(3) OF 21 ...I ===> A...



I (3) A
YIELD 81%

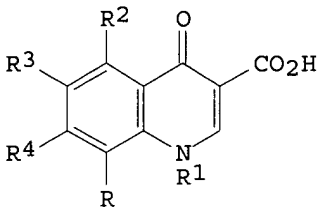
RX(3) RCT I 118959-66-3
RGT J 7646-69-7 NaH
PRO A 111279-72-2
SOL 109-99-9 THF

L7 ANSWER 35 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 113:58966 CASREACT
TITLE: Quinolonecarboxylic acid derivatives and their preparation as bactericides
INVENTOR(S): Masuzawa, Kuniyoshi; Suzue, Seigo; Hirai, Keiji; Ishizaki, Takayoshi
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 26,194, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4894458	A	19900116	US 1988-233363	19880818
JP 62215572	A	19870922	JP 1986-59016	19860317
PRIORITY APPLN. INFO.:			JP 1986-59016	19860317
			US 1987-26194	19870316

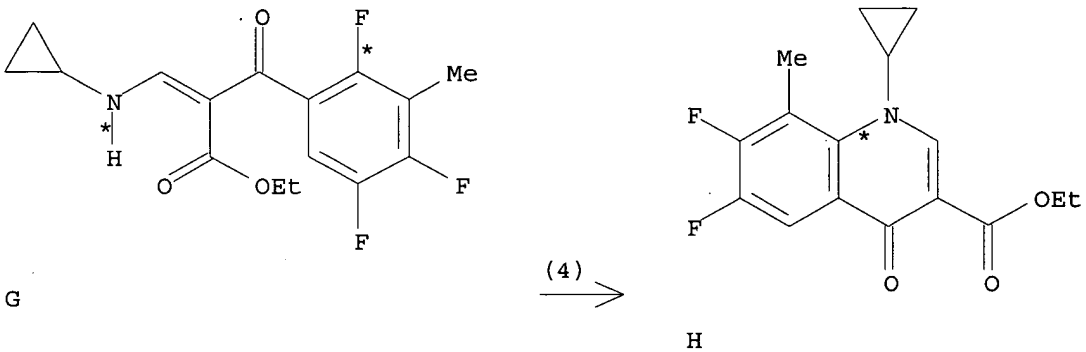
OTHER SOURCE(S): MARPAT 113:58966
GI



I

AB Title compds. I (R = alkyl; R1 = C3-6 cycloalkyl, alkyl, haloalkyl, alkenyl, hydroxyalkyl, alkylamino, Ph; R2 = H, halo, O2N, H2N; R3 = halo; R4 = halo, azetidino, pyrrolidino, piperidino, (thio)morpholino, (un)substituted (homo)piperazino, etc.) and pharmaceutically acceptable salts, are prepared I (R = Me, R1 = cyclopropyl, R2 = H, R3 = R4 = F), 3-tert-butoxycarbonylaminopyrrolidine, DBU and anhydrous MeCN were refluxed for 18 h to give I (R = Me, R1 = cyclopropyl, R2 = H, R3 = F, R4 = 3-amino-2-pyrrolidinyl) (II). In vitro against Bacillus subtilis the min. inhibitory concentration of II was 0.025 μg/mL vs. 0.05 μg/mL for ciprofloxacin.

RX(4) OF 68 ...G ===> H...



G

H

RX(4) RCT G 112822-90-9
PRO H 112822-91-0

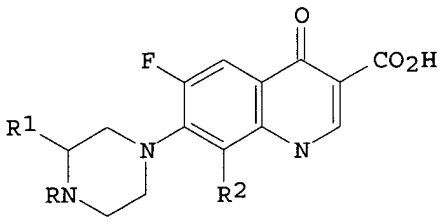
L7 ANSWER 36 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 112:179026 CASREACT
TITLE: 7-Piperazinyl-4-oxoquinoline-3-carboxylic acids as bactericides
INVENTOR(S): Ueda, Hiraki; Miyamoto, Hisashi; Aki, Shinji; Otsuka, Tatsuya
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: U.S., 19 pp. Cont.-in-part of U.S. Ser. No. 17,247, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4874764	A	19891017	US 1987-63401	19870618
SE 8700527	A	19870826	SE 1987-527	19870211
SE 501371	C2	19950123		
JP 63264461	A	19881101	JP 1987-37000	19870219
JP 07053715	B	19950607		
KR 9700950	B1	19970121	KR 1987-1600	19870225
AU 603352	B2	19901115	AU 1987-69767	19870306
AU 8769767	A	19880908		
US 4855292	A	19890808	US 1987-76888	19870723
US 4880806	A	19891114	US 1987-76890	19870723
US 4935420	A	19900619	US 1988-259471	19881017

PRIORITY APPLN. INFO.:

JP 1986-40921	19860225
JP 1986-105655	19860508
JP 1986-118568	19860522
JP 1986-173370	19860723
JP 1986-193838	19860819
JP 1986-233837	19860930
JP 1986-246050	19861015
JP 1986-303515	19861218
JP 1987-37000	19870219
US 1987-17247	19870220
US 1987-76889	19870723

OTHER SOURCE(S): MARPAT 112:179026
GI

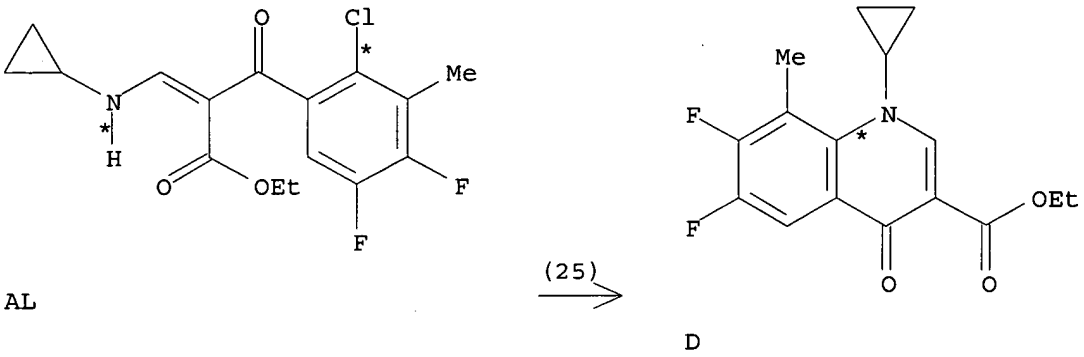


I

AB Title compds. I (R = H; R1, R2 = alkyl) are prepared Treatment of 6,7-difluoro-1-cyclopropyl-8-Me-1,4-dihydro-4-oxoquinoline-3-carboxylic acid-B(OAc)2 chelate (preparation given) with 4-benzyl-3-methylpiperazine and dimethylacetamide gave I (R = PhCH2; R1 = R2 = ME), which in AcOH was hydrogenated in the presence of Pd/C to afford I (R = H; R1 = R2 = Me).

The latter showed MIC's of 0.2 and 0.2 (no unit is given) against Staphylococcus aureus and Bacteroides ilimosum.

RX(25) OF 216 ...AL ===> D...



AL

D

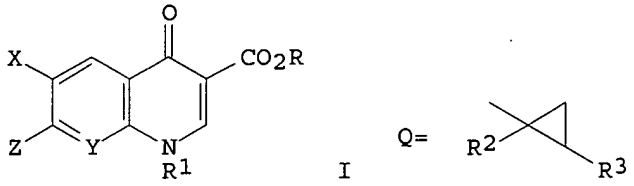
RX(25) RCT AL 126483-96-3
RGT AM 7646-69-7 NaH
PRO D 112822-91-0

L7 ANSWER 37 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 112:118793 CASREACT
TITLE: Preparation of 1-tert-alkylnaphthyridine and -quinolinecarboxylic acids as antibacterial agents
INVENTOR(S): Di Cesare, Pierre; Jacquet, Jean Pierre; Essiz, Munir; Remuzon, Philippe; Bouzard, Daniel; Weber, Abraham
PATENT ASSIGNEE(S): Bristol-Myers Co., USA
SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 266576	A2	19880511	EP 1987-114686	19871008
EP 266576	A3	19890322		
R: ES, GR				
PL 154473	B1	19910830	PL 1987-268098	19871007
PL 156484	B1	19920331	PL 1987-287459	19871007
CN 87106925	A	19880914	CN 1987-106925	19871008
CS 270597	B2	19900712	CS 1987-7295	19871008
CS 270598	B2	19900712	CS 1988-7400	19881110
US 4965273	A	19901023	US 1988-278638	19881201
US 4954507	A	19900904	US 1988-287502	19881219

PRIORITY APPLN. INFO.: US 1986-916752 19861008
US 1987-99231 19870925
CS 1987-7295 19871008

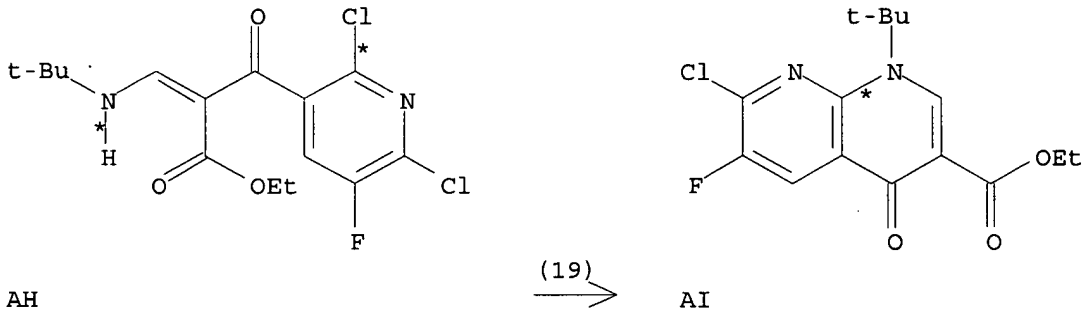
OTHER SOURCE(S): MARPAT 112:118793
GI



I

AB The title compds. [I; R = H; R1 = Me3C, EtCMe2, PhCMe2, CH2:CMe, 1-methylcyclobutyl, 1-adamantyl, cyclopropyl moiety Q; all of which may be substituted by 1-3 halo atoms; R2 = Me, Ph; R3 = H, Me; X = Br, Cl, F, CF3, CCl3; Y = CH, CBr, CCl, CF, N; Z = (un)substituted pyrrolidino, piperazino, (thio)morpholino, bicyclic amino] and their pharmaceutically acceptable acid or base salts were prepared as bactericides. (R,R)-2,5-Diazabicyclo[2.2.1]heptene-2HBr, prepared in 7 steps from 4-hydroxy-D-proline Et ester-HCl, was refluxed with Et 1-(1,1-dimethylethyl)-7-chloro-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylate (preparation given) in pyridine containing 1,8-diazabicyclo[5.4.0]undec-7-ene to give I [R = Et, R1 = Me3C, X = F, Y = N, Z = (R,R)-2,5-diazabicyclo[2.2.1]hept-2-yl)which was saponified to give I (R = H, other groups unchanged), isolated as its methanesulfonate salt (II). II had a min. inhibitory concentration of 0.06 μg/mL against Staphylococcus aureus and Escherichia coli.

RX(19) OF 204 ...AH ===> AI...



AH AI

RX(19) RCT AH 116163-45-2
RGT AJ 7646-69-7 NaH
PRO AI 116163-18-9

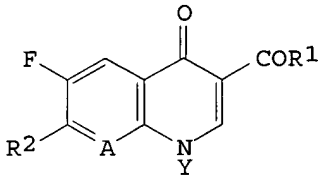
L7 ANSWER 38 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 112:77161 CASREACT
TITLE: Preparation of 6-fluoro-1,4-dihydro-4-oxo-(1,8-naphthyridine or quinoline)-3-carboxylic acid derivatives as antibacterial agents
INVENTOR(S): Brighty, Katherine E.; Lowe, John Adams, III; McGuirk, Paul Robert
PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

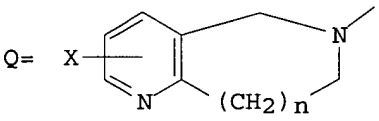
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 321191	A2	19890621	EP 1988-311797	19881214
EP 321191	A3	19910227		
EP 321191	B1	19941102		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
WO 8905643	A1	19890629	WO 1987-US3412	19871218
W: FI, HU, NO, RO, SU, US				
HU 50469	A2	19900228	HU 1987-1279	19871218
IL 88664	A	19930818	IL 1988-88664	19881212
ES 2061695	T3	19941216	ES 1988-311797	19881214
ZA 8809395	A	19900829	ZA 1988-9395	19881215
AU 8826987	A	19890622	AU 1988-26987	19881216
AU 600188	B2	19900802		
DK 8806997	A	19890811	DK 1988-6997	19881216
JP 01211587	A	19890824	JP 1988-319341	19881216
JP 07025757	B	19950322		
FI 8903883	A	19890817	FI 1989-3883	19890817
FI 90239	B	19930930		
FI 90239	C	19940110		
NO 8903305	A	19891017	NO 1989-3305	19890817
NO 178149	B	19951023		
NO 178149	C	19960131		

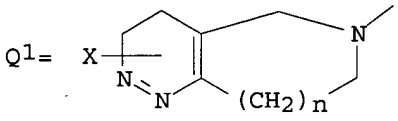
PRIORITY APPLN. INFO.: WO 1987-US3412 19871218

GI



I

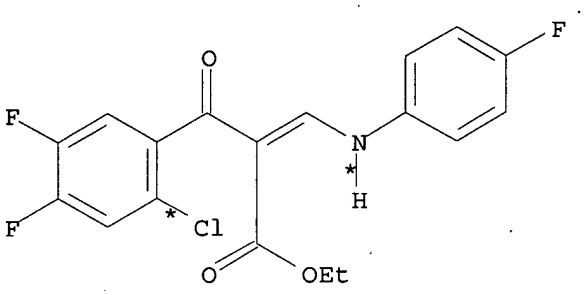




AB The title compds. [I; Y = C1-3 (hydroxy, fluoro, or chloro)alkyl, cyclopropyl, 2,4-F2C6H3, 4-FC6H4; A = CH, CF, CCl, COMe, N; or A = C and AY = CZCH2CR3 or CZCH2C(:CH2); Z = O, CH2; R3 = H, C1-3 alkyl, FCH2, ClCH2; R1 = OH, C1-6 alkoxy, (C1-6 alkyl)amino, OM; M = pharmaceutically acceptable cation; R2 = heterocyclyl, e.g. Q, Q1; X = H, 1 or 2 of CH2NHR4, NHR4 or C1-6 alkylsulfonyl; R4 = H, C1-6 alkyl; n = 0, 1] are prepared as antibacterial agents (no data). Thus, a solution of 2-amino-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine in Me2SO was treated with 1-cyclopropyl-6,7-difluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid and heated to 80° overnight to give 94% 7-[5-(2-amino-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridyl)]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-

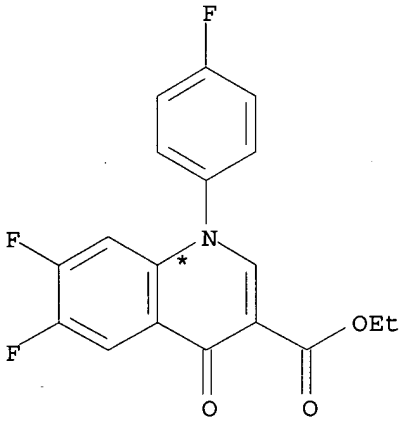
oxoquinoline-3-carboxylic acid.

RX(7) OF 41 ...M ===> K...



M

(7)



K
YIELD 90%

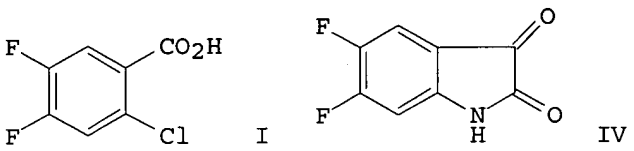
RX(7) RCT M 124458-08-8
PRO K 108138-16-5

L7 ANSWER 39 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 111:173772 CASREACT
TITLE: Process for preparing 2-chloro-4,5-difluorobenzoic acid, an intermediate for antibacterial quinolinecarboxylic acid derivatives
INVENTOR(S): Bitha, Panayota; Lin, Yang I.
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4833270	A	19890523	US 1987-136052	19871221

PRIORITY APPLN. INFO.: US 1987-136052 19871221

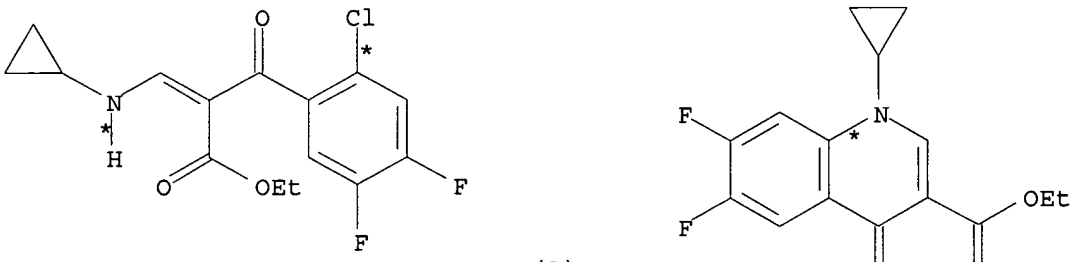
GI



I IV

AB 2-Chloro-4,5-difluorobenzoic acid (I), an intermediate for quinolinecarboxylic acid derivs. useful as antibacterials, is prepared from 3,4-F2C6H3NH2 (II) via 3,4-F2C6H3NHCOCH:NOH (III), 5,6-difluoro-1H-indole-2,3-dione (IV), and 2-amino-4,5-difluorobenzoic acid (V). A mixture of II, chloral hydrate, NH2OH.HCl, Na2SO4, concentrated HCl, and H2O was refluxed for 2 h and filtered hot to collect solid III, which was cyclized in concentrated H2SO4 at 80° to give IV. Ring cleavage of IV by treatment in 2.5 N NaOH with H2O2 and then acid workup gave V, which was treated with anhydrous CuCl2 and tert-Bu nitrite in dry MeCN at 0-5°, followed by addition to 6N HCl, to give I. This was converted to 1-cyclopropyl-6,7-difluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid in 6 addnl. steps.

RX(2) OF 66 ...C ===> A...



C A

RX(2) RCT C 127371-49-7
PRO A 98349-25-8

L7 ANSWER 40 OF 103 CASREACT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 111:97219 CASREACT
Correction of: 104:129888

TITLE: 1,4-Dihydro-4-oxonaphthyridine derivatives and their salts, with antibacterial properties

INVENTOR(S): Narita, Hirokazu; Konishi, Yoshinori; Nitta, Jun; Nagaki, Hideyoshi; Kitayama, Isao; Kobayashi, Yoriko; Shinagawa, Mikako; Watanabe, Yasuo; Yotsuji, Akira; et al.

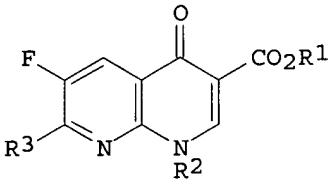
PATENT ASSIGNEE(S): Toyama Chemical Co., Ltd., Japan
SOURCE: Ger. Offen., 74 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3514076	A1	19851031	DE 1985-3514076	19850418
DE 3514076	C2	19890330		
JP 60228479	A	19851113	JP 1984-84963	19840426
JP 63020828	B	19880430		
DE 3546658	C2	19920402	DE 1985-3546658	19850418
NL 8501172	A	19851118	NL 1985-1172	19850423
NL 187314	B	19910318		
NL 187314	C	19910816		
GB 2158825	A	19851120	GB 1985-10297	19850423
GB 2158825	B	19890125		
NO 8501643	A	19851028	NO 1985-1643	19850424
NO 162238	B	19890821		
NO 162238	C	19891206		
AU 8541650	A	19851031	AU 1985-41650	19850424
AU 565087	B2	19870903		
DD 238795	A5	19860903	DD 1985-275518	19850424
RO 91871	B3	19870730	RO 1985-118517	19850424
RO 95509	B3	19880930	RO 1985-126286	19850424
AT 8501224	A	19890615	AT 1985-1224	19850424
AT 389698	B	19900110		
IL 75021	A	19940125	IL 1985-75021	19850424
BE 902279	A1	19851025	BE 1985-214909	19850425
DK 8501856	A	19851027	DK 1985-1856	19850425
DK 165877	B	19930201		
DK 165877	C	19930621		
FI 8501637	A	19851027	FI 1985-1637	19850425
FI 80453	B	19900228		
FI 80453	C	19900611		
SE 8502017	A	19851027	SE 1985-2017	19850425
SE 463102	B	19901008		
SE 463102	C	19910207		
FR 2563521	A1	19851031	FR 1985-6327	19850425
FR 2563521	B1	19890203		
HU 38634	A2	19860630	HU 1985-1599	19850425
HU 194226	B	19880128		
ES 542584	A1	19860916	ES 1985-542584	19850425
ZA 8503102	A	19861230	ZA 1985-3102	19850425
CS 250684	B2	19870514	CS 1985-3035	19850425
HU 197571	B	19890428	HU 1987-3675	19850425
CH 673458	A5	19900315	CH 1985-1798	19850425
PL 147392	B1	19890531	PL 1985-253108	19850426
JP 61137819	A	19860625	JP 1985-239522	19851028
JP 62037006	B	19870810		
JP 61143383	A	19860701	JP 1985-239523	19851028
JP 05078556	B	19931029		
CS 250698	B2	19870514	CS 1985-8906	19851205
ES 551538	A1	19870701	ES 1986-551538	19860131
GB 2191776	A	19871223	GB 1987-16897	19870717
GB 2191776	B	19900328		
JP 63132888	A	19880604	JP 1987-254530	19871012

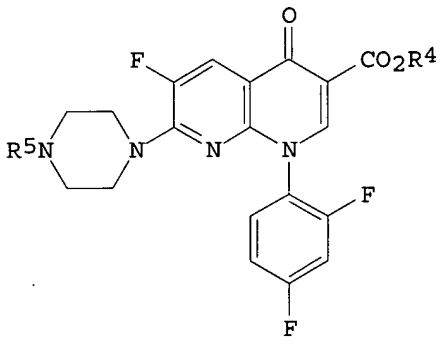
JP 06033262	B	19940502		
AU 8781804	A	19880324	AU 1987-81804	19871125
AU 612993	B2	19910725		
FR 2614620	A1	19881104	FR 1988-8836	19880630
FR 2614620	B1	19900309		
AT 8802678	A	19890915	AT 1988-2678	19881031
AT 390258	B	19900410		
SE 8804586	A	19881220	SE 1988-4586	19881220
SE 501412	C2	19950213		
NL 9100647	A	19910801	NL 1991-647	19910415
NL 192574	B	19970602		
NL 192574	C	19971003		
NL 9100648	A	19910801	NL 1991-648	19910415
PRIORITY APPLN. INFO.:			JP 1984-84963	19840426
			GB 1985-10297	19850423
			NL 1985-1172	19850423
			AT 1985-1224	19850424
			CS 1985-3035	19850425

OTHER SOURCE(S): MARPAT 111:97219

GI



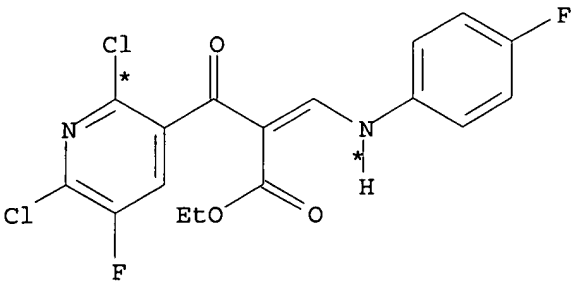
I



II

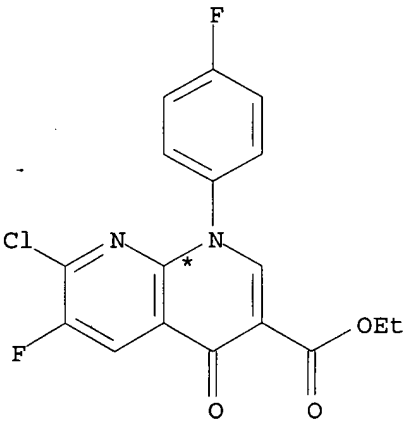
AB The title 1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylates I [R1 = H, protective group; R2 = (un)substituted aryl; R3 = N-attached, saturated heterocyclyl] (>80 compds.) were prepared Thus, 2,6-dichloro-5-fluoronicotinic acid was converted to its acid chloride and condensed with EtOCH(CO2Et)2 Mg salt to give, after decarboxylation, Et (2,6-dichloro-5-fluoronicotinoyl)acetate. The latter was condensed with 2,4-difluoroaniline and Me2NCH(OEt)2 to give Et 2-(2,6-dichloro-5-fluoronicotinoyl)-3-(2,4-difluoroanilino)acrylate which was cyclized by heating at 120° in DMF containing NaHCO3 to give I (R1 = Et, R2 = 2,4-F2C6H3, R3 = Cl). This was heated at 60° with 1-acetylpiperazine in CHCl3 to give piperazinylnaphthylridinecarboxylate II (R4 = Et, R5 = Ac) which was refluxed in 6N HCl to give II (R4 = R5 = H). The I are effective bactericides with min. inhibitory concns. ≤0.05 μg/mL against, e.g., Staphylococcus aureus F137.

RX(3) OF 65 ...F ===> G



F

(3) →



G

RX(3) RCT F 100491-00-7
PRO G 100491-30-3

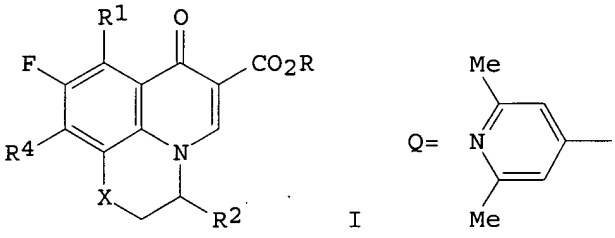
L7 ANSWER 41 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 111:78016 CASREACT
TITLE: Preparation and testing of 9-fluoro-6-oxo-10-pyridinylpyrido[1,2,3-de][1,4]benzoxazine-6-carboxylates and -benzothiazine-6-carboxylates as antimicrobials
INVENTOR(S): Lesher, George Yohe
PATENT ASSIGNEE(S): Sterling Drug Inc., USA
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 306860	A2	19890315	EP 1988-114389	19880902
EP 306860	A3	19900718		

R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE					
US 4839355	A	19890613	US 1988-220717	19880718
IL 87553	A	19920525	IL 1988-87553	19880824
ZA 8806402	A	19890426	ZA 1988-6402	19880829
AU 8821718	A	19890309	AU 1988-21718	19880831
AU 599829	B2	19900726		
NO 8803898	A	19890310	NO 1988-3898	19880901
DK 8804940	A	19890310	DK 1988-4940	19880906
FI 8804107	A	19890310	FI 1988-4107	19880906
JP 01139583	A	19890601	JP 1988-224385	19880907
PRIORITY APPLN. INFO.:			US 1987-94611	19870909
			US 1988-220717	19880718

OTHER SOURCE(S): MARPAT 111:78016

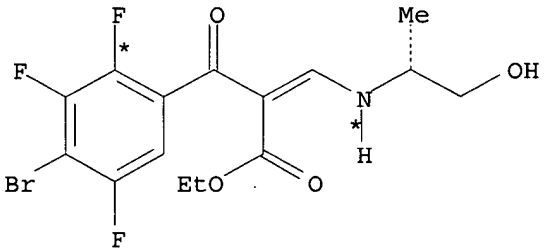
GI



I

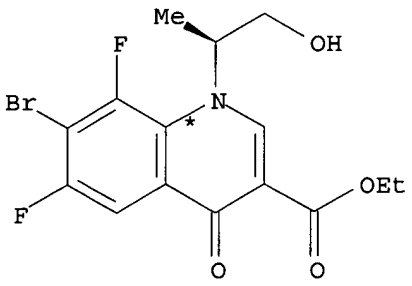
AB The title compds. (I; R = H, alkyl; R1 = H, F, SR3; R2 = C1-3 alkyl; R3 = alkyl, Ph, PhCH2; R4 = Q; X = O, S) (II), useful as antibacterials, were prepared Et S-10-bromo-8,9-difluoro-3-methyl-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylate (preparation from Et 4-bromo-2,3,5,6-tetrafluorobenzoylacetate and S-2-amino-1-propanol given), 2,6-dimethyl-4-trimethylsilylstannylpyridine, and HMPA in dioxane were treated with (Ph3P)2PdCl2 and the mixture was refluxed 24 h. The product was refluxed 2 h with 1 M HCl to give I (R = H, R1 = F, R2 = Me, R4 = Q, X = O). II had min. inhibitory concs. of 0.25- <0.004 μg/mL against Staphylococcus aureus.

RX(24) OF 95 ...M ===> AT...



M

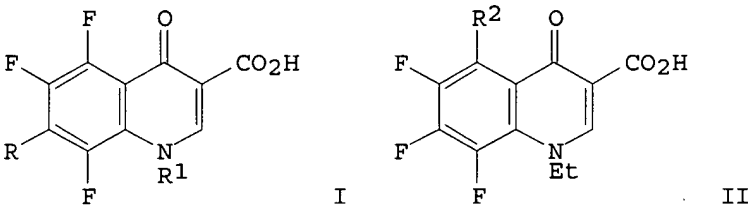
(24)



AT

RX(24) RCT M 122033-64-1
PRO AT 122033-67-4
CAT 554-13-2 Li2CO3

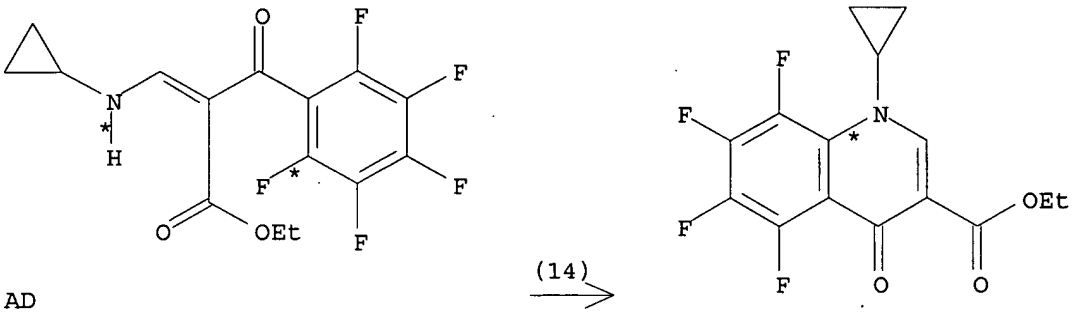
L7 ANSWER 42 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 110:231413 CASREACT
TITLE: Synthesis of novel 5-fluoro analogs of norfloxacin and ciprofloxacin
AUTHOR(S): Moran, Daniel B.; Ziegler, Carl B., Jr.; Dunne, Theresa S.; Kuck, Nydia A.; Lin, Yang I.
CORPORATE SOURCE: Med. Res. Div., Am. Cyanamid Co., Pearl River, NY, 10965, USA
SOURCE: Journal of Medicinal Chemistry (1989), 32(6), 1313-18
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I II

AB 7-Amino-5,6,8-trifluoro-3-quinolonecarboxylic acid derivs. I (R = N-methylpiperazino, R1 = Et, CHMe2, cyclopropyl, C6H4F-p; R = morpholino, pyrrolidino, thiomorpholino, R1 = Et) and 5-amino-6,7,8-trifluoroquinolonecarboxylic acids II (R2 = morpholino, N-methylpiperazino) were prepared and tested for bactericidal activity in vitro and in vivo in mice. I were prepared regioselectively by amination of the corresponding 5,6,7,8-tetrafluoroquinolonecarboxylic acids, while II were prepared regioselectively by amination of the corresponding Et 5,6,7,8-tetrafluoroquinolonecarboxylates. Antibacterial activity was greatest for I (R = N-methylpiperazino, R1 = cyclopropyl). II were inactive in vitro.

RX(14) OF 57 ...AD ===> AE...

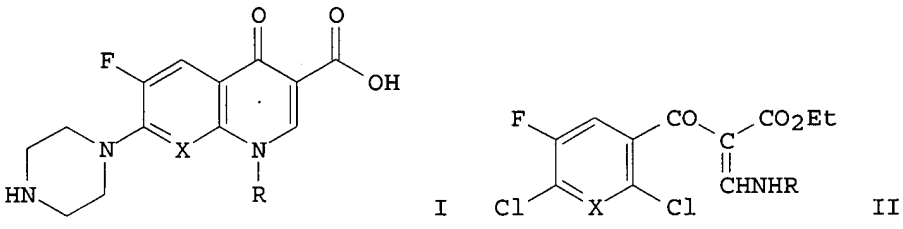


AD

AE
YIELD 96%

RX(14) RCT AD 107564-01-2
RGT AF 584-08-7 K2CO3
PRO AE 107564-02-3
SOL 68-12-2 DMF

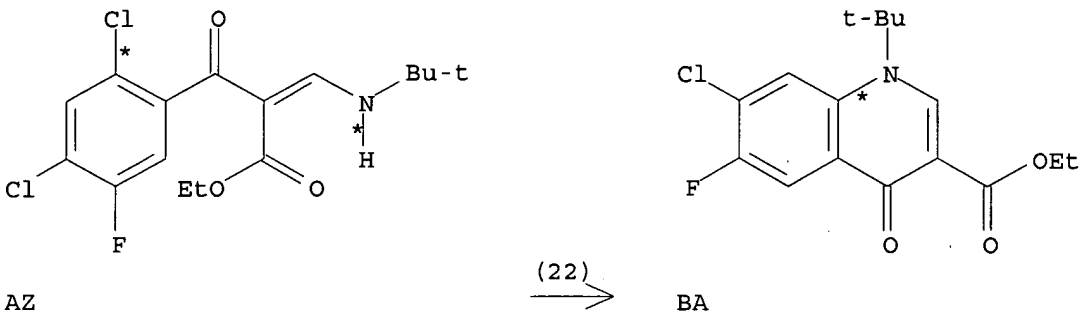
L7 ANSWER 43 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 110:154185 CASREACT
TITLE: Fluoronaphthyridines and quinolones as antibacterial agents. 1. Synthesis and structure-activity relationship of new 1-substituted derivatives
AUTHOR(S): Bouzard, D.; Di Cesare, P.; Essiz, M.; Jacquet, J. P.; Remuzon, P.; Weber, A.; Oki, T.; Masuyoshi, M.
CORPORATE SOURCE: Cent. Rech., Bristol-Myers, Torcy, 77422, Fr.
SOURCE: Journal of Medicinal Chemistry (1989), 32(3), 537-42
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I II

AB The quinolones and naphthyridines I (R = alkyl, alkenyl, cycloalkyl, cycloalkenyl, arylalkyl; X = CH, CF, N) were prepared by cyclization of aroylaminoacrylates II, followed by hydrolysis of the ester and substitution by piperazine. The in vitro and in vivo antibacterial activity is greatest for I (R = CMe3; X = CH, N) especially against Staphylococcus aureus Smith A 9537, which was better than ciprofloxacin (I; R = cyclopropyl, X = CH).

RX(22) OF 69 AZ ===> BA...



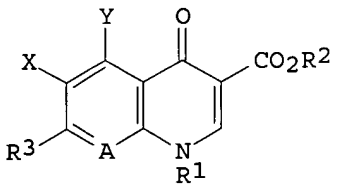
AZ BA

RX(22) RCT AZ 116163-40-7
RGT D 7646-69-7 NaH
PRO BA 116163-44-1
SOL 123-91-1 Dioxane

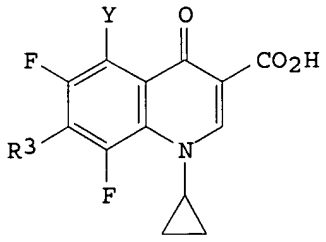
L7 ANSWER 44 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 110:114697 CASREACT
TITLE: Preparation of 5-substituted quinolone- and naphthyridonecarboxylic acids as antibacterial agents
INVENTOR(S): Petersen, Uwe; Grohe, Klaus; Schriewer, Michael; Schenke, Thomas; Haller, Ingo; Metzger, Karl; Endermann, Rainer; Zeiler, Hans Joachim
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 32 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3711193	A1	19881013	DE 1987-3711193	19870402
NO 8801121	A	19881003	NO 1988-1121	19880314
EP 284935	A1	19881005	EP 1988-104452	19880321
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
AU 8813811	A	19881006	AU 1988-13811	19880328
DD 274029	A5	19891206	DD 1988-314159	19880329
DK 8801802	A	19881003	DK 1988-1802	19880330
FI 8801501	A	19881003	FI 1988-1501	19880330
CN 88101741	A	19881116	CN 1988-101741	19880331
ZA 8802318	A	19881228	ZA 1988-2318	19880331
JP 63258855	A	19881026	JP 1988-78298	19880401
HU 47098	A2	19890130	HU 1988-1619	19880401
HU 201050	B	19900928		

PRIORITY APPLN. INFO.: DE 1987-3711193 19870402
OTHER SOURCE(S): MARPAT 110:114697
GI



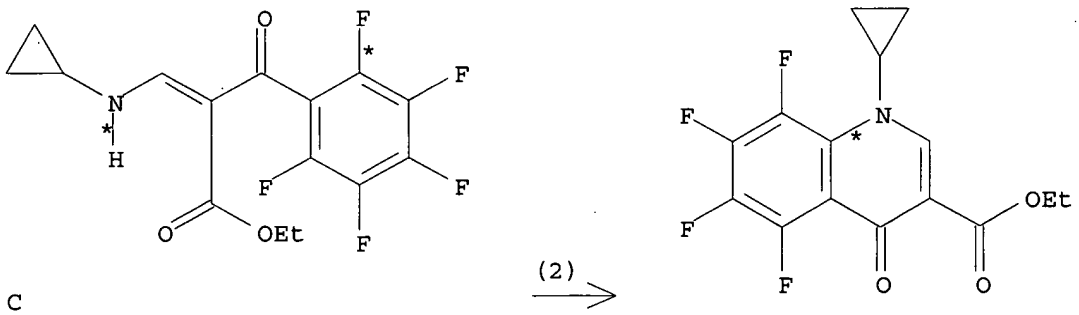
I



II

AB The title compds. [I; A = N, CR9; R1 = Me, Et, cyclopropyl, etc.; R2 = H, alkyl, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl; R3 = Me, 13 N-attached heterocyclyl; R9 = H, halo, Me, cyano, NO2; R1R9 = OCH2CHMe, SCH2CHMe, CH2CH2CHMe] were prepared C6F5COCH2CO2Et (preparation given) was refluxed 2 h with HC(OEt)3 in Ac2O to give C6F5COC(CO2Et):CHOEt which was treated overnight with cyclopropylamine in EtOH to give C6F5COC(CO2Et):CHNHR (R = cyclopropyl). The latter was refluxed 3 h in DMF containing NaF to give, after saponification, quinolonecarboxylate II (R3 = Y = F) which was refluxed 3 h with 1-methylpiperazine in MeCN/DMF containing Dabco to give II (R3 = 4-methyl-1-piperazinyl, Y = F) (III). Tablets were prepared each containing III 583.0, cellulose 55.0, starch 72.0, polyvinylpyrrolidone 30.0, SiO2 5.0, and Mg stearate 5.0 mg with a coating comprising (hydroxypropyl)methylcellulose 6.0, Macrogol 40,000 2.0, and TiO2 2.0 mg. II (R3 = 3-methyl-1-piperazinyl, Y = NH2) had a min. inhibitory concentration of 0.5 (units not given) against Escherichia coli 455/7.

RX(2) OF 42 C ===> D...



C

D

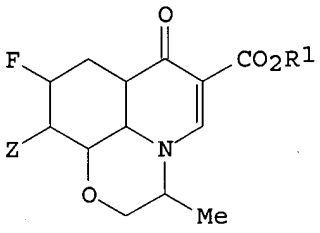
RX(2) RCT C 107564-01-2
PRO D 107564-02-3

L7 ANSWER 45 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 110:75530 CASREACT
TITLE: Process for preparation of racemic and optically active ofloxacin and related derivatives
INVENTOR(S): Mitscher, Lester A.; Chu, Daniel T.
PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4777253	A	19881011	US 1986-858532	19860425
US 4826985	A	19890502	US 1988-216063	19880707

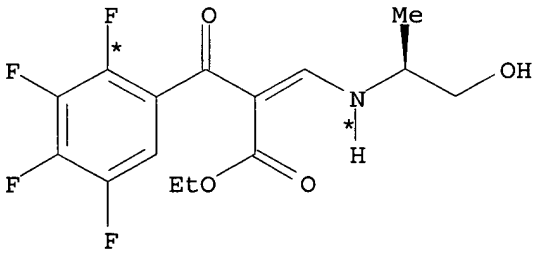
PRIORITY APPLN. INFO.: US 1986-858532 19860425
OTHER SOURCE(S): MARPAT 110:75530
GI



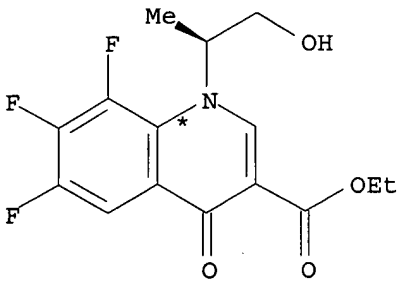
I

AB The title compds. I (R1 = H, C1-4 alkyl, PhCH2; Z = R4R5N; R4, R5 = H, alkanoyl, alkanoylamido, substituted amino; R4R5N = (un)substituted aliphatic heterocyclyl) (wherein the the racemate of ofloxacin exhibits antibacterial properties) were prepared (-)-I (R1 = Et; Z = F) (preparation given) in pyridine was added to 1-methylpiperazine, the mixture heated to 55°, and after workup, the solid obtained was dissolved in THF and NaOH solution to give (-)-I (R1 = H; Z = 4-methylpiperazinyl).

RX(7) OF 102 ...L ===> D...



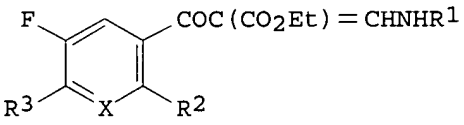
L (7) →



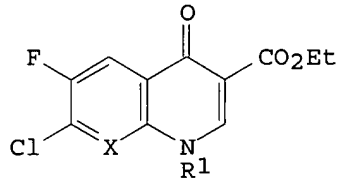
D

RX(7) RCT L 110548-02-2
PRO D 110548-03-3

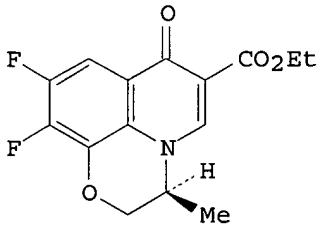
L7 ANSWER 46 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 110:57479 CASREACT
TITLE: Use of tetrabutylammonium fluoride as a cyclization agent in the synthesis of bactericidal 4-pyridone-3-carboxylic acid derivatives
AUTHOR(S): Bouzard, D.; Di Cesare, P.; Essiz, M.; Jacquet, J. P.; Remuzon, P.
CORPORATE SOURCE: Centr. Rech., Bristol-Myers, Marne La Vallee, 77422, Fr.
SOURCE: Tetrahedron Letters (1988), 29(16), 1931-4
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: French
GI



I



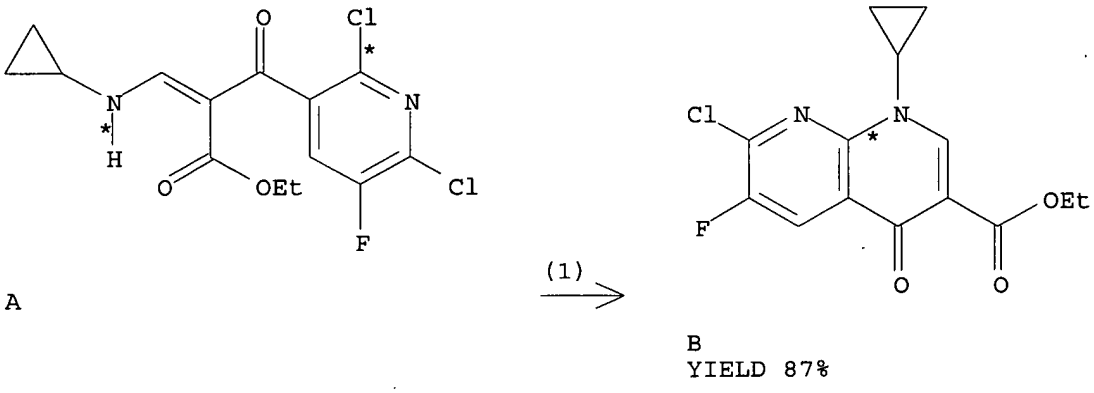
II



III

AB Bu2NF catalyzed the cyclization of enamines I (X = N, CH, CF; R1 = cyclopropyl, 4-FC6H4, Me3CSiMe2OCH2CHMe; R2, R3 = Cl, F) to pyridone derivs. II (same R1) and III. III is a key intermediate in the synthesis of (S)-Ofloxacin.

RX(1) OF 5 A ===> B



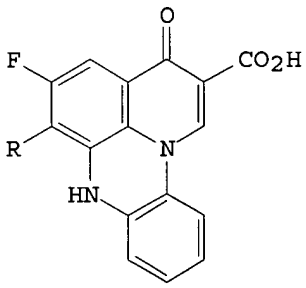
A

(1)

B
YIELD 87%

RX(1) RCT A 96568-06-8
PRO B 96568-07-9
CAT 429-41-4 Bu4N.F
SOL 109-99-9 THF

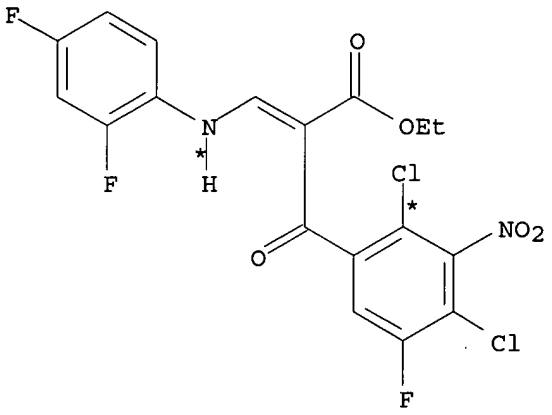
L7 ANSWER 47 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 109:190368 CASREACT
TITLE: Synthesis of 4,12-dihydro-4-oxoquino[1,8a,8-a,b]quinoxaline-5-carboxylic acid derivatives
AUTHOR(S): Chu, Daniel T. W.; Maleczka, Robert E., Jr.; Nordeen, Carl W.
CORPORATE SOURCE: Anti-Infective Res. Div., Abbott Lab., Abbott Park, IL, 60064, USA
SOURCE: Journal of Heterocyclic Chemistry (1988), 25(3), 927-30
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



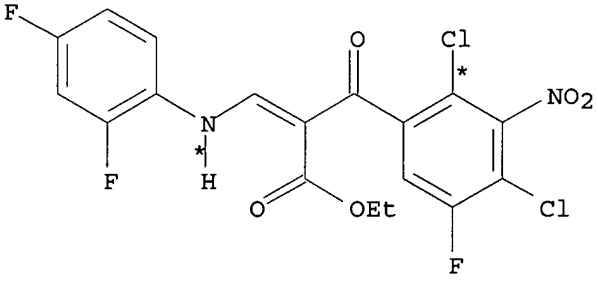
I

AB The synthesis and antibacterial activity of title compds. I (R = 3-amino-1-pyrrolidinyl, 4-methyl-1-piperazinyl) are described. The synthetic route includes a carbon homologation and 2 intramol. nucleophilic displacement cyclizations.

RX(4) OF 75 ...L + M ===> 2 Q...

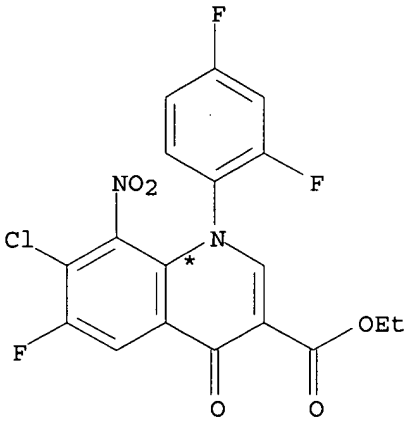


L

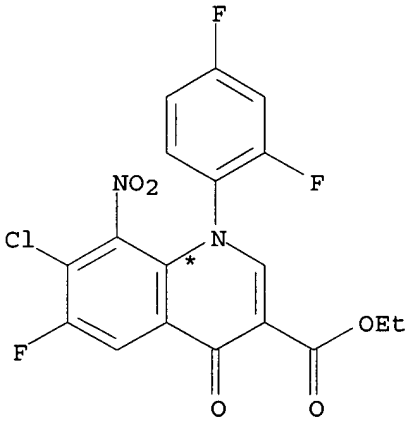


M

(4)



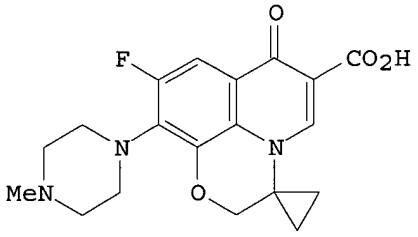
Q
YIELD 79%



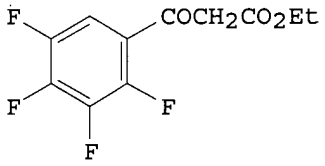
Q
YIELD 79%

RX(4) RCT L 117239-44-8, M 117239-35-7
RGT R 7646-69-7 NaH
PRO Q 117239-36-8
SOL 109-99-9 THF

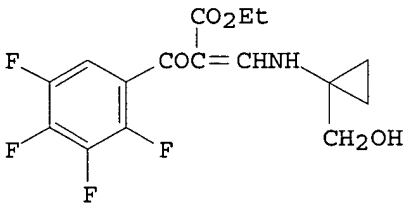
L7 ANSWER 48 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 109:92905 CASREACT
TITLE: Synthesis and bacterial DNA gyrase inhibitory properties of a spirocyclopropylquinolone derivative
AUTHOR(S): Wentland, Mark P.; Perni, Robert B.; Dorff, Peter H.; Rake, James B.
CORPORATE SOURCE: Dep. Med. Chem. Microbiol., Sterling-Winthrop Res. Inst., Rensselaer, NY, 12144, USA
SOURCE: Journal of Medicinal Chemistry (1988), 31(9), 1694-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



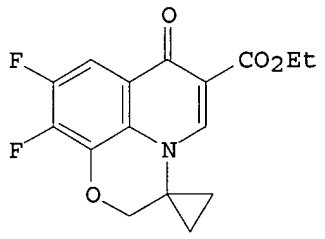
I



II



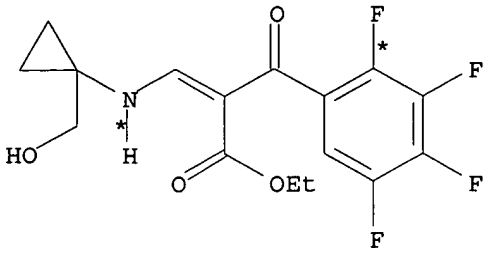
III



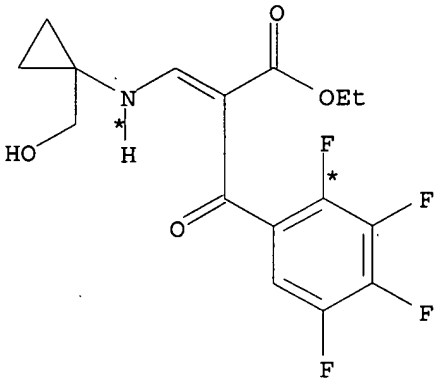
IV

AB A novel conformationally restricted 1-cyclopropylquinlone, I, that incorporates structural features of both ofloxacin and ciprofloxacin was prepared from ester II via cyclopropyl derivative III. Cyclization of III with K2CO3-DMF gave 66% pyridobenzoxazine derivative IV. Ester hydrolysis of IV followed by substitution with N-methylpiperazine gave I. I was a DNA gyrase inhibitor having potency similar to ofloxacin but less than ciprofloxacin. The cellular inhibitory and in vivo antibacterial potencies of I were less than those of the two reference agents.

RX(7) OF 113 ...U + V ===> 2 X...

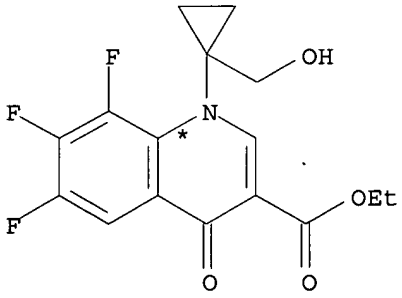


U

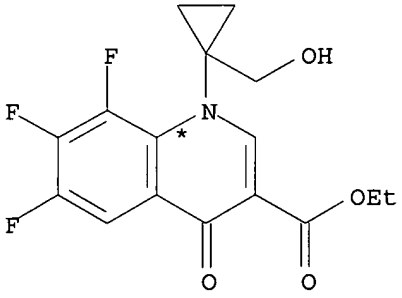


V

(7)



X
YIELD 88%



X
YIELD 88%

RX(7) RCT U 114636-47-4, V 114636-48-5
RGT Y 7646-69-7 NaH
PRO X 113211-50-0
SOL 109-99-9 THF

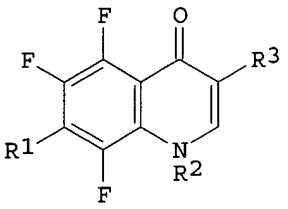
L7 ANSWER 49 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 109:92822 CASREACT
TITLE: Preparation of trifluoroquinolinecarboxylic acid derivatives as antibacterial agents
INVENTOR(S): Teraji, Tsutomu; Matsushima, Hiroshi; Yamamura, Atsushi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 247464	A1	19871202	EP 1987-107108	19870516
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8703565	A	19871230	ZA 1987-3565	19870518
JP 63002979	A	19880107	JP 1987-120784	19870518
AU 8773172	A	19871126	AU 1987-73172	19870519
PRIORITY APPLN. INFO.:			GB 1986-12137	19860519

OTHER SOURCE(S): MARPAT 109:92822

GI



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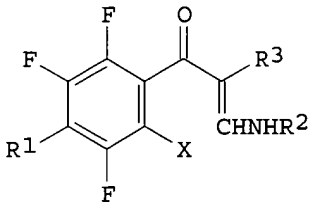
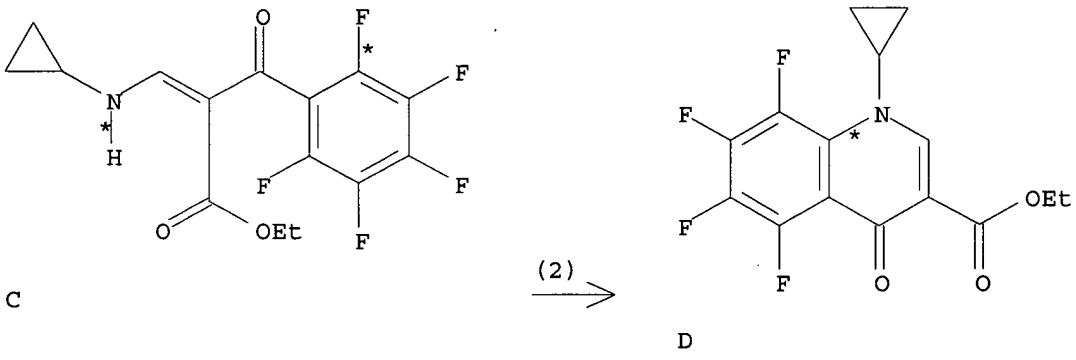


II

AB The title compds. I [R1 = di(lower)alkylamino, piperazinyl (substituted with lower alkyl), morpholinyl, pyrrolidinyl, or piperidyl; R2 = cyclo(lower)alkyl, Ph having lower alkyl and OH; R3 = (protected) CO2H], useful as bactericides, were prepared from II (X = halo). Condensation of Et 2-ethoxymethylene-3-(2,3,4,5,6-pentafluorophenyl)-3-oxopropionate (preparation given) with cyclopropylamine, followed by cyclization, hydrolysis, and amination with piperazine, gave I (R1 = 1-piperazinyl, R2 = cyclopropyl, R3 = CO2H) (III). III in vitro exhibited a MIC of 0.10 μg/mL against Mycoplasma pulmonis PG-22.

RX(2) OF 16 ...C ===> D...



C

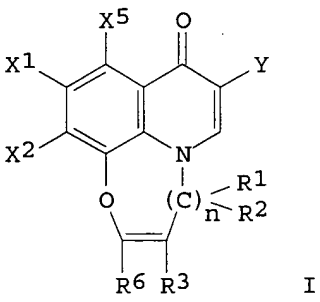
D

RX(2) RCT C 107564-01-2
PRO D 107564-02-3

L7 ANSWER 50 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 109:86326 CASREACT
TITLE: 1,8-Bridged 4-quinolonecarboxylic acids, their preparation and bactericidal pharmaceuticals containing them
INVENTOR(S): Schriewer, Michael; Grohe, Klaus; Hagemann, Hermann; Zeiler, Hans Joachim; Metzger, Karl Georg
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3623757	A1	19880121	DE 1986-3623757	19860715
US 4816451	A	19890328	US 1987-68074	19870629
EP 253235	A1	19880120	EP 1987-109593	19870703
EP 253235	B1	19910102		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
AT 59654	T	19910115	AT 1987-109593	19870703
ES 2031854	T3	19930101	ES 1987-109593	19870703
JP 63039880	A	19880220	JP 1987-174999	19870715
PRIORITY APPLN. INFO.:			DE 1986-3623757	19860715
			EP 1987-109593	19870703

OTHER SOURCE(S): MARPAT 109:86326
GI

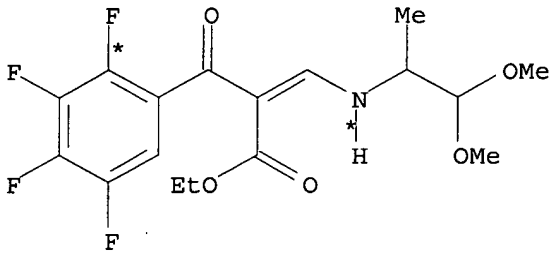


I

AB 1,8-Bridged 4-quinolone derivs. [I: R1-R3, R6 = H, (un)substituted alkyl, alkoxy, alkylmercapto, aryl, 5- or 6-membered (un)substituted heterocyclic ring; Y = CO2, nitrile, CO2R7, CONR8R9; R7 = C1-4 alkyl; R8, R9 = (un)substituted Ph; X1 = H, NO2, alkyl, halo, preferably F; X2 = NR10R11; R10, R11 = (un)substituted heterocyclic 5- or 6-membered ring which optionally containing other heteroatoms; n = 0,1] are bactericides. Et 3-ethoxy-2-(2,3,4,5-tetrafluorobenzoyl)acrylate (6.4 g) was treated with 2.6 g 1-aminopropionaldehyde diacetal in 15 mL EtOH to give 8 g Et 2-(2,3,4,5-tetrafluorobenzoyl)-3-(1-methyl-2,2-dimethoxy-1-methylethylamino)acrylate. This (64 g) was cyclized in the presence of 24 g K2CO3 in 370 mL DMF to give 42 g Et quinolinecarboxylate; the latter (4.4) was hydrolyzed in the presence of 15 mL AcOH, 13 mL H2O and 1.3 mL H2SO4 to give 3.0 g of the corresponding aldehyde. The product (2.2 g)

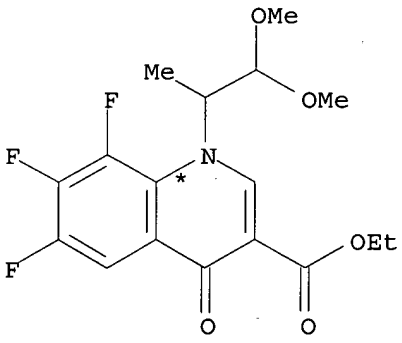
was cyclized in the presence of 0.6 g NaOH in 20 mL 6-carboxylic acid, and 1.6 g of this was treated with 2.9 g N-methylpiperazine in 20 mL DMSO to give 0.4 g I (X1 = F, X2 = piperazinyl, X5 = H, Y = CO2H, R3 = Me, R6 = H).

RX(2) OF 10 ...C ===> D...



C

(2)



D

RX(2) RCT C 115841-51-5
PRO D 115841-52-6

=> d ibib abs fhit 51-103
NO VALID FORMATS ENTERED FOR FILE 'PS'
In a multifile environment, each file must have at least one valid format requested. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):ibib abs fhit 51-88
'51-88' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> d his

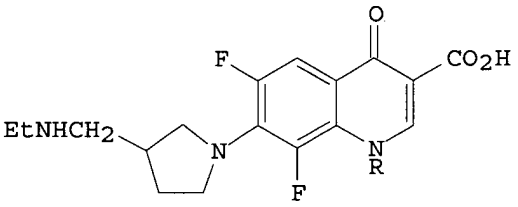
(FILE 'HOME' ENTERED AT 10:05:33 ON 19 DEC 2006)

FILE 'CASREACT, CHEMINFORMRX, DJSMONLINE, PS' ENTERED AT 10:05:55 ON 19 DEC 2006

L1 STRUCTURE UPLOADED
L2 11 S L1
L3 104 S L1
L4 283 S L3 AND POTASSIUM PHOSPHATE TRIBASIC OR (K3PO4)
L5 1 S L3 AND((POTASSIUM PHOSPHATE TRIBASIC) OR (K3PO4))
L6 0 S L3 AND (ORGANIC SOLVENT)
L7 103 S L3 NOT L5

=> d ibib abs fhit 51-70

L7 ANSWER 51 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 108:167270 CASREACT
TITLE: 1-Substituted 7-[3-[(ethylamino)methyl]-1-pyrrolidinyl]-6,8-difluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acids. New quantitative structure activity relationships at N1 for the quinolone antibacterials
AUTHOR(S): Domagala, John M.; Heifetz, Carl L.; Hutt, Marland P.; Mich, Thomas F.; Nichols, Jeffry B.; Solomon, Marjorie; Worth, Donald F.
CORPORATE SOURCE: Parke-Davis Pharm. Res. Div., Warner-Lambert Co., Ann Arbor, MI, 48105, USA
SOURCE: Journal of Medicinal Chemistry (1988), 31(5), 991-1001
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

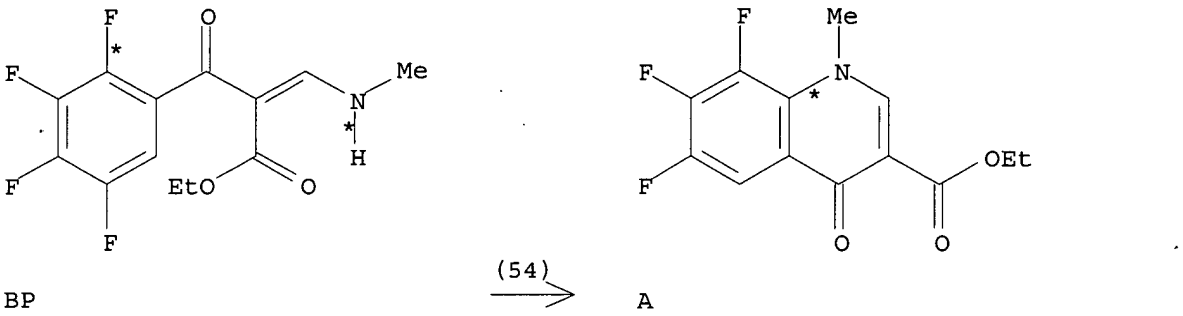


I

AB A series of 18 1-substituted 7-[3-[(ethylamino)methyl]-1-pyrrolidinyl]-6,8-difluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acids, e.g. I (R = Me, Et, etc.) (N1 analogs of CI-934) were synthesized and evaluated for antibacterial activity and DNA-gyrase inhibition. Correlations between the inhibition of DNA gyrase and antibacterial potency were established. A quant. structure-activity relationship (QSAR) was derived by using the antibacterial potency for each of 11 strains of bacteria and the Gram-neg. mean. The equations indicated that antibacterial potency was strongly dependent on STERIMOL length and width and the level of unsatn. of the N1 substituent. Some strains also showed a dependence on the presence of heteroatoms (O, N, S) in the N1 group. No significant correlations between gyrase inhibition and combinations of these parameters were found. These QSAR results are discussed in conjunction with the conformational analyses from mol. modeling studies. The substituent that most enhanced the activity of the quinolone in all regards was the cyclopropyl group. This analog, 1-cyclopropyl-7-[3-[(ethylamino)methyl]-1-pyrrolidinyl]-6,8-

difluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid (PD 117558), demonstrated outstanding broad spectrum activity both in vitro and in vivo when compared to relevant stds.

RX(54) OF 298 ...BP ===> A...



BP A

RX(54) RCT BP 113220-15-8
RGT DB 865-47-4 t-BuOK
PRO A 113220-28-3
SOL 75-65-0 t-BuOH

L7 ANSWER 52 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 108:150325 CASREACT
TITLE: Preparation of trifluoroquinolonecarboxylic acid derivatives as medical bactericides
INVENTOR(S): Matsumoto, Junichi; Miyamoto, Teruyuki; Egawa, Hiroshi; Nakamura, Shinichi
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 65 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 242789	A2	19871028	EP 1987-105602	19870415
EP 242789	A3	19900905		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DD 263290	A5	19881228	DD 1987-302040	19870422
FI 8701788	A	19871026	FI 1987-1788	19870423
AU 8771909	A	19871029	AU 1987-71909	19870423
ZA 8702874	A	19871230	ZA 1987-2874	19870423
DK 8702087	A	19871026	DK 1987-2087	19870424
NO 8701727	A	19871026	NO 1987-1727	19870424
JP 63045261	A	19880226	JP 1987-102586	19870424
JP 2572591	B2	19970116		
HU 45520	A2	19880728	HU 1987-1795	19870424
HU 198198	B	19890828		
SU 1627086	A3	19910207	SU 1987-4202458	19870424
CN 87103138	A	19871104	CN 1987-103138	19870425
US 4886810	A	19891212	US 1987-42806	19870427
SU 1582986	A3	19900730	SU 1988-4355430	19880328

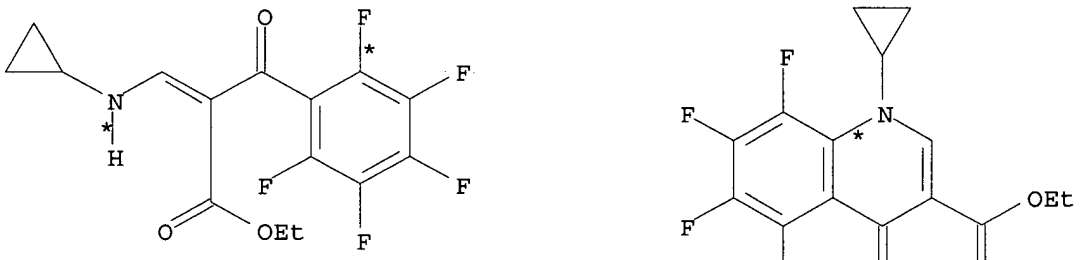
SU 1588281	A3	19900823	SU 1988-4355417	19880330
SU 1588282	A3	19900823	SU 1988-4355529	19880418

PRIORITY APPLN. INFO.: JP 1986-97543 19860425
OTHER SOURCE(S): MARPAT 108:150325
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I (Z = amino, halo; R = Q1, Q2 wherein R1 = H, alkyl, haloalkyl; R2 = H, alkyl; R3 = alkyl, haloalkyl; R4 = H, alkyl; R5, R6 = H, alkyl, or NR5R6 = heterocyclyl; n = 0 or 1, with the proviso that when Z is amino, R is Q2), useful as medical bactericides, were prepared via: (a) reaction of II (X = halo; Y = H, aliphatic group; Z = as given above, with the proviso that when Z is halo, Y is H) with RH (R = as given above); (b) reaction of II (X = R; Z = halo; Y = as given above) with NH3 (c) solvolysis or hydrogenolysis of II [Z = (protected) amino, halo; X = Q1, Q2 which may bear a protected amino group, with the proviso that at least either Z is a protected amino group or Q1 or Q2 bears an amino-protecting group, etc.]; (d) cyclization of III (Y = aliphatic group; X = halo; R, Z = as defined above). A mixture of 1-cyclopropyl-5,6,7,8-tetrafluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid (preparation given) and 2-methylpiperazine in pyridine was stirred at 80° for 1 h to give I (Z = F, R = 3-methyl-1-piperazinyl) (IV). IV in vitro exhibited a min. inhibitory concentration of 0.2 μg/mL against S. aureus 209P JC-1.

RX(2) OF 6 ...D ===> E...

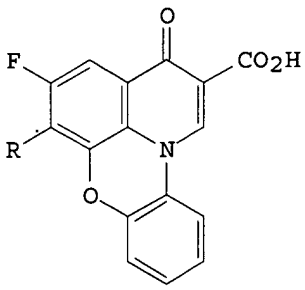


D E

RX(2) RCT D 107564-01-2
RGT F 7646-69-7 NaH
PRO E 107564-02-3

L7 ANSWER 53 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 108:5940 CASREACT
TITLE: Synthesis of 4-oxo-4H-quino[2,3,4-i,j][1,4]benoxazine-5-carboxylic acid derivatives
AUTHOR(S): Chu, Daniel T. W.; Maleczka, Robert E., Jr.
CORPORATE SOURCE: Anti-Infect. Res. Div., Abbott Lab., North Chicago, IL, 60064, USA

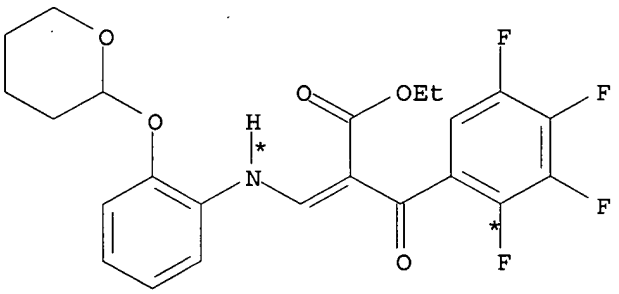
SOURCE: Journal of Heterocyclic Chemistry (1987), 24(2), 453-6
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

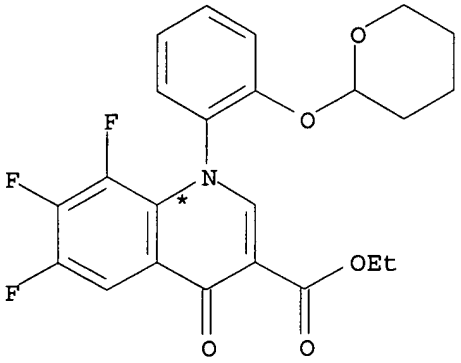
AB The synthesis and antibacterial activity of quinobenoxazine-5-carboxylic acids I (R = piperazinyl, 4-methylpiperazinyl, 3-methylpyrrolidinyl) is described. Key steps in the synthesis include carbon homologation and two intramol. nucleophilic displacement cyclization reactions to generate the 4-oxo-4H-quino[2,3,4-i,j]-[1,4]benoxazine-5-carboxylic acid nucleus. I showed good broad spectrum antibacterial activity against 5 gram-pos. and 6 gram-neg. bacteria, but they are slightly less potent than their uncyclized arylquinolone analog.

RX(5) OF 71 ...Q ===> S...



Q

(5)



S
YIELD 65%

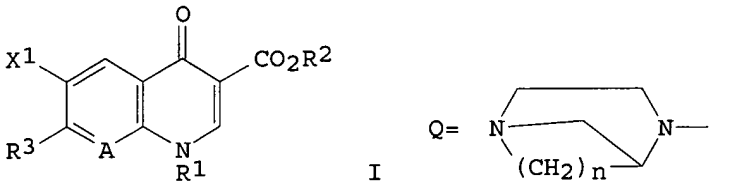
RX(5) RCT Q 111783-49-4
RGT T 7646-69-7 NaH
PRO S 111783-50-7
SOL 109-99-9 THF

L7 ANSWER 54 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 107:236747 CASREACT
TITLE: Preparation of 7-(azabicycloalkyl)-3-quinolinecarboxylates and -3-naphthyridinecarboxylates as bactericides and feed additives
INVENTOR(S): Petersen, Uwe; Grohe, Klaus; Schenke, Thomas; Hagemann, Hermann; Zeiler, Hans Joachim; Metzger, Karl Georg
PATENT ASSIGNEE(S): Bayer A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

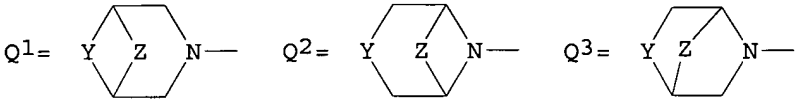
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3601567	A1	19870723	DE 1986-3601567	19860121
AU 8767463	A	19870723	AU 1987-67463	19870109
NO 8700126	A	19870722	NO 1987-126	19870113
EP 230274	A2	19870729	EP 1987-100460	19870115
EP 230274	A3	19880309		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
SU 1538897	A3	19900123	SU 1987-4028796	19870115
FI 8700200	A	19870722	FI 1987-200	19870119
DD 265401	A5	19890301	DD 1987-299333	19870119
DK 8700292	A	19870722	DK 1987-292	19870120
ZA 8700380	A	19870930	ZA 1987-380	19870120
JP 62169789	A	19870725	JP 1987-10113	19870121
CN 87100354	A	19870902	CN 1987-100354	19870121
HU 45531	A2	19880728	HU 1987-178	19870121
PRIORITY APPLN. INFO.:			DE 1986-3601567	19860121

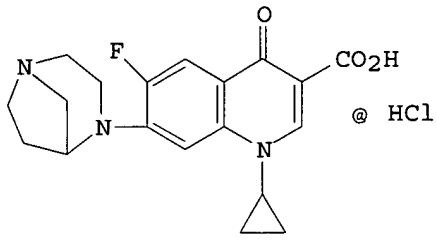
OTHER SOURCE(S): MARPAT 107:236747

GI



I

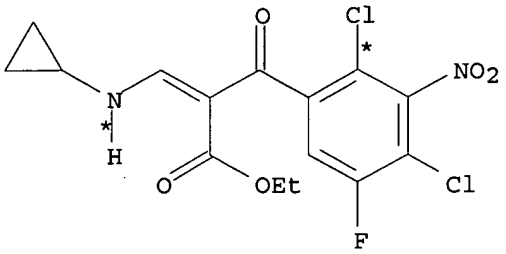




II

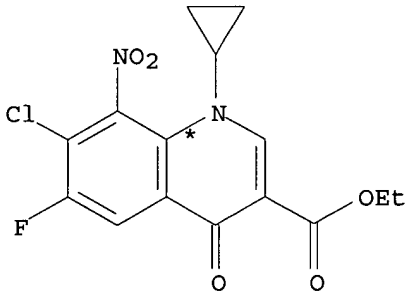
AB The title compds. [I; A = N, R4C; R1 = Me, Et, Pr, Me2CH, cyclopropyl, CH2:CH, HOCH2CH2, FCH2CH2, MeO, Ph, FC6H4, 2,4-F2C6H3, NH2, MeNH, Me2N; R2 = H, C1-4 alkyl, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl; R3 = Q-Q3, optionally substituted by OH, Me; R4 = H, Me, Cl, F, NO2, R1R4 = OCH2CHMe, SCH2CHMe, CH2CH2CHMe; X1 = Cl, F, NO2; Y = R5N, O, S; R5 = H, C2-4 oxoalkyl, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, (OH-substituted) C1-4 alkyl, alkenyl, alkynyl, (un)substituted PhCH2; Z = (CH2)n, CH2OCH2, CH2SCH2, CH2S, CH2,NR6CH2; R6 = H, Me; n = 1-3] were prepared as bactericides and feed additives. 1-Cyclopropyl-6,7-difluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid and 1,4-diazabicyclo[3.2.1]octane were refluxed 6 h in MeCN/DMF in the presence of 1,4-diazabicyclo[2.2.2]octane to give, after acidification, diazabicyclooctylquinoline carboxylate II. II had a min. inhibitory concentration of 0.125 mcg/mL against Staphylococcus aureus 133 compared to 0.5 mcg/mL for ciprofloxacin. Tablets were prepared each containing II 583.0, microcryst. cellulose 55.0, cornstarch 72.0, polyvinylpyrrolidone 30.0, colloidal silica 5.0, Mg stearate 5.0, (hydroxypropyl)methylcellulose 6.0, macrogol 4000 2.0, and TiO2 2.0 mg.

RX(4) OF 5 G ===> C...



G

(4)



C

RX(4) RCT G 111453-56-6
PRO C 111453-55-5

L7 ANSWER 55 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 107:236733 CASREACT
TITLE: Preparation of piperazinylquinolonecarboxylates as bactericides
INVENTOR(S): Matsumoto, Junichi; Miyamoto, Teruyuki; Egawa, Hiroshi; Nakamura, Shinichi
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 50 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 221463	A2	19870513	EP 1986-114748	19861023
EP 221463	A3	19871202		
EP 221463	B1	19910814		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 8664277	A	19870430	AU 1986-64277	19861022
AU 594983	B2	19900322		
FI 8604299	A	19870430	FI 1986-4299	19861023
FI 87457	B	19920930		

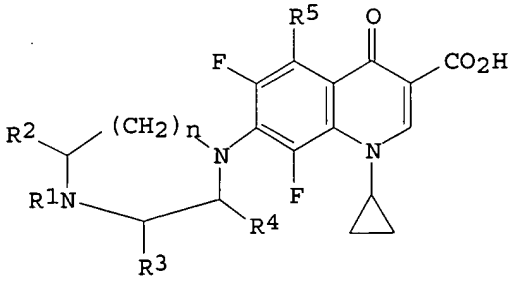
FI 87457	C	19930111		
NO 8604247	A	19870430	NO 1986-4247	19861023
NO 170726	B	19920817		
NO 170726	C	19921125		
IL 80404	A	19900610	IL 1986-80404	19861023
EP 375658	A1	19900627	EP 1990-101210	19861023
EP 375658	B1	19940803		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 66210	T	19910815	AT 1986-114748	19861023
ES 2029786	T3	19921001	ES 1986-114748	19861023
ES 2057197	T3	19941016	ES 1990-101210	19861023
ZA 8608094	A	19870624	ZA 1986-8094	19861024
HU 43839	A2	19871228	HU 1986-4479	19861024
SU 1519529	A3	19891030	SU 1986-4028442	19861027
DK 8605145	A	19870430	DK 1986-5145	19861028
DK 170593	B1	19951106		
JP 62277362	A	19871202	JP 1986-257175	19861028
JP 05041633	B	19930624		
DD 254006	A5	19880210	DD 1986-295648	19861028
US 4795751	A	19890103	US 1986-928297	19861028
CA 1340402	C	19990223	CA 1986-521561	19861028
CN 86107491	A	19870429	CN 1986-107491	19861029
CN 1009930	B	19901010		
CS 277409	B6	19930317	CS 1986-7833	19861029
SU 1598873	A3	19901007	SU 1987-4203548	19871027
SU 1635898	A3	19910315	SU 1987-4203544	19871027
JP 05043551	A	19930223	JP 1991-359794	19911226
JP 07014918	B	19950222		
NO 9200721	A	19870430	NO 1992-721	19920224
NO 173993	B	19931122		
NO 173993	C	19940302		
DK 9200259	A	19920228	DK 1992-259	19920228
DK 170774	B1	19960115		
FI 9202482	A	19920529	FI 1992-2482	19920529
FI 89797	B	19930813		
FI 89797	C	19931125		

PRIORITY APPLN. INFO.:

JP 1985-242257	19851029
JP 1985-285323	19851217
JP 1986-32627	19860217
EP 1986-114748	19861023
FI 1986-4299	19861023
NO 1986-4247	19861023

OTHER SOURCE(S): MARPAT 107:236733

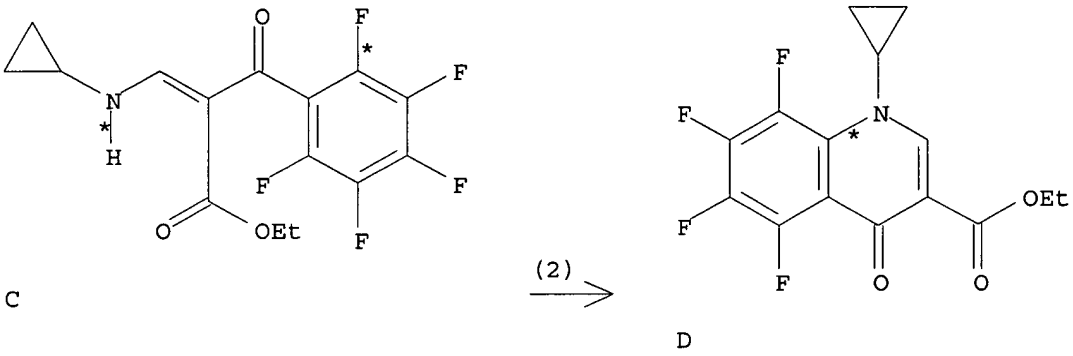
GI



I

AB The title compds. (I; R1 = H, Me, Et; R2 = H, Me, CH2F; R3, R4 = H, Me; R5 = halo, amino; n = 1, 2) were prepared as bactericides. 5-Amino-1-cyclopropyl-6,7,8-trifluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid (1.25 g) was heated with 2.0 g 2-methylpiperazine in pyridine at 105-110° for 1 h to give 1.4 g I (R1 = R2 = R4 = H, R3 = Me, R5 = NH2) (II). II inhibited S. aureus Number 80 with a MIC of 0.0125 μg/mL. Capsules were prepared containing II 250, starch 50, lactose 35, and talc 15 g/1000 capsules.

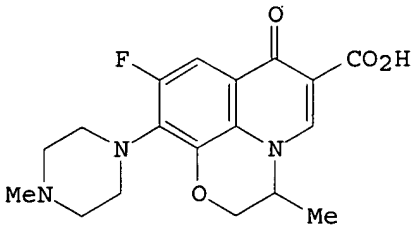
RX(2) OF 29 ...C ===> D...



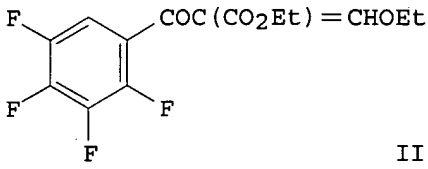
C D

RX(2) RCT C 107564-01-2
PRO D 107564-02-3

L7 ANSWER 56 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 107:198206 CASREACT
TITLE: Chiral DNA gyrase inhibitors. 2. Asymmetric synthesis and biological activity of the enantiomers of 9-fluoro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid (ofloxacin)
AUTHOR(S): Mitscher, Lester A.; Sharma, Padam N.; Chu, Daniel T. W.; Shen, Linus L.; Pernet, Andre G.
CORPORATE SOURCE: Dep. Med. Chem., Kansas Univ., Lawrence, KS, 66045, USA
SOURCE: Journal of Medicinal Chemistry (1987), 30(12), 2283-6
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



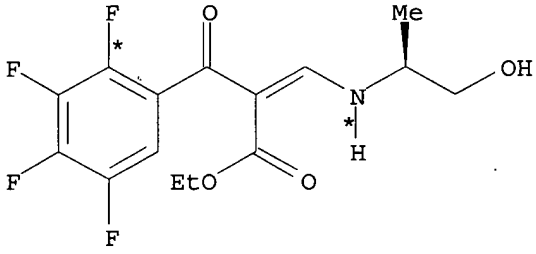
I



II

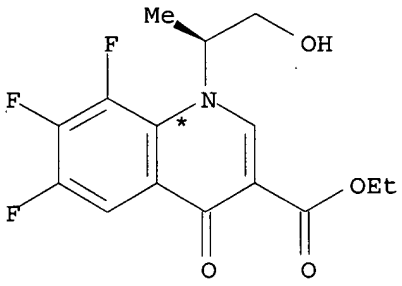
AB A short and efficient synthesis of the two optical antipodes of ofloxacin (I) from (R)- and (S)-alaninol and (tetrafluorobenzoyl)alkene II is reported. In vitro testing of the products against a range of bacteria and in an assay system incorporating purified DNA gyrase from different bacterial species demonstrates that the S-(-) enantiomer is substantially the more active.

RX(3) OF 37 ...F ===> H...



F

(3) →



H
YIELD 59%

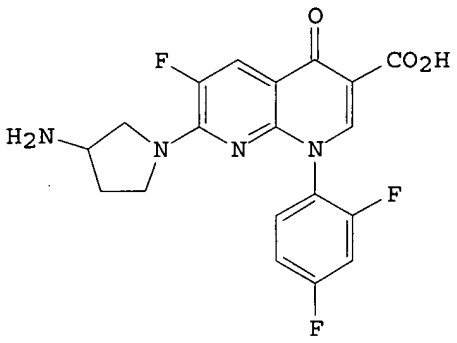
RX(3) RCT F 110548-02-2
RGT I 7646-69-7 NaH
PRO H 110548-03-3
SOL 67-68-5 DMSO

L7 ANSWER 57 OF 103 CASREACT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 107:183566 CASREACT
TITLE: Bactericides: 7-(3-amino-1-pyrrolidinyl)-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthylidine-3-carboxylic acid, or its salt, and C2-6 organic acids
INVENTOR(S): Ohashi, Osamu; Takakura, Isamu; Kitani, Akinori; Niimura, Tetsuzo; Narita, Hirokazu; Takamichi, Akira; Saikawa, Isamu
PATENT ASSIGNEE(S): Toyama Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62072616	A	19870403	JP 1985-214145	19850927
JP 02034324	B	19900802		
PRIORITY APPLN. INFO.:			JP 1985-214145	19850927

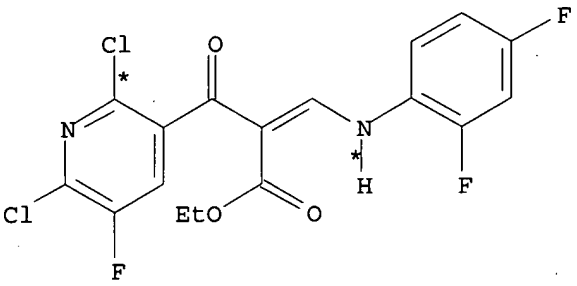
GI



I

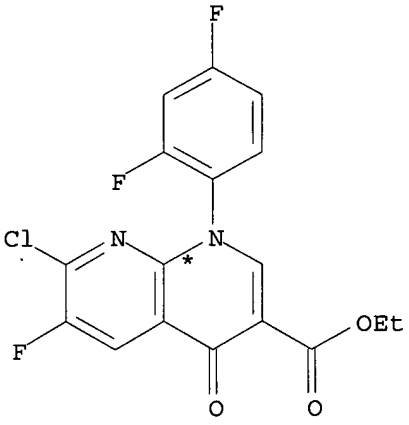
AB Absorption of the naphthylidine derivative (I) or its salt from the digestive tract is improved by administration with C2-6 organic acids. I 4-toluenesulfonate 50 and citric anhydride 50 g were mixed and sifted through a 24-mesh net. The powder was mixed with 1 g Mg stearate and encapsulated (50 mg I 4-toluenesulfonate/capsule).

RX(1) OF 2 A ===> B



A

(1) →



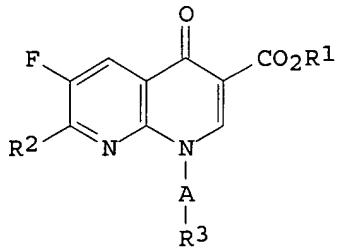
B

RX(1) RCT A 100490-99-1
PRO B 100491-29-0

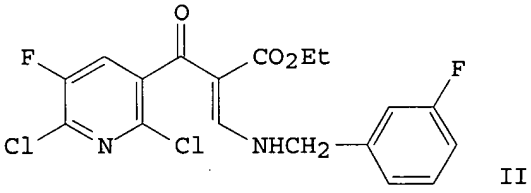
L7 ANSWER 58 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 107:134294 CASREACT
TITLE: Preparation of 6-fluoro-1,4-dihydro-1,8-naphthyridine-3-carboxylate derivatives as antibacterial agents
INVENTOR(S): Narita, Hirokazu; Konishi, Yoshinori; Nitsuta, Jun; Takagi, Hiroyasu; Iino, Fumihiko; Kobayashi, Junko; Saikawa, Isamu
PATENT ASSIGNEE(S): Toyama Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62084085	A	19870417	JP 1985-225515	19851009
JP 07017642	B	19950301		

JP 07196657 A 19950801 JP 1994-218015 19940819
JP 2630566 B2 19970716
PRIORITY APPLN. INFO.: JP 1985-225515 19851009
GI



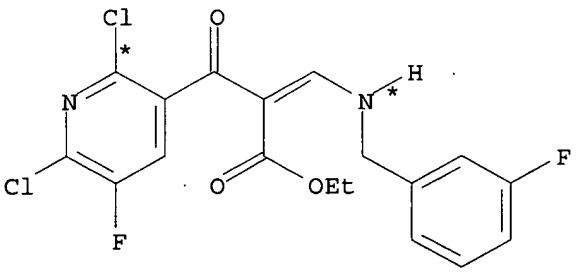
I



II

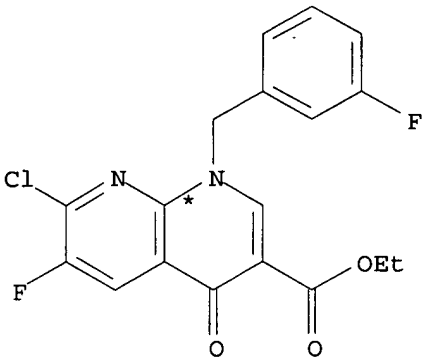
AB The title compds. [I; R1 = H, protecting group; R2 = halo, (un)substituted cyclic amino; R3 = (un)substituted aryl or heterocyclyl; A = NH, alkylimino, alkenylene, alkylene optionally substituted by halo, OH, alkanesulfonyloxy or arenesulfonyloxy] and their salts, useful as antibacterial agents, were prepared A a mixture of 3.0 g Et 2,6-dichloro-5-fluoronicotinoyl acetate, 4.37 g Ac2O and 6.35 g CH(OEt)3 was refluxed for 1 h and the solvent was removed in vacuo. The residue was treated with 1.38 g m-FC6H4CH2NH2 in EtOH for 1 h to give 92.2% a pyridine derivative II, which was cyclized by NaHCO3 in DMF at 120° to give 93.8% I (R1 = Et, R2 = Cl, R3A = m-FC6H4CH2NH) (III). Reaction of III with 3-aminopyrrolidine-2HCl in EtOH-CHCl3 gave, after hydrolysis with aqueous HCl, I (R1 = H, R2 = 3-amino-1-pyrrolidinyl, R3A = m-FC6H4CH2NH).HCl. This in vitro was active against bacteria, e.g., Staphylococcus aureus, with MIC of 0.39 μg/mL.

RX(1) OF 38 A ===> B



A

(1) →



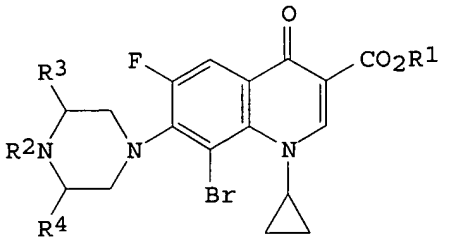
B

RX(1) RCT A 110286-35-6
PRO B 110286-53-8

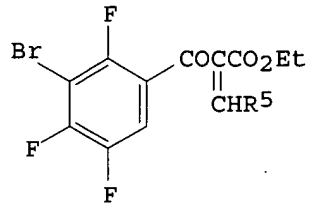
L7 ANSWER 59 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 107:58883 CASREACT
TITLE: Preparation of quinolinecarboxylic acid derivatives as antibacterials
INVENTOR(S): Masuzawa, Kuniyasu; Suzue, Seigo; Hirai, Keiji; Ishizaki, Takayoshi
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62059263	A	19870314	JP 1985-200240	19850910
US 4826982	A	19890502	US 1986-902606	19860902
AU 8662400	A	19870312	AU 1986-62400	19860904
AU 577712	B2	19880929		
CA 1262135	A1	19891003	CA 1986-517708	19860908
CN 86106169	A	19870318	CN 1986-106169	19860909
CN 1010313	B	19901107		
EP 216245	A1	19870401	EP 1986-112471	19860909
EP 216245	B1	19900725		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
HU 44026	A2	19880128	HU 1986-3888	19860909
HU 197893	B	19890628		

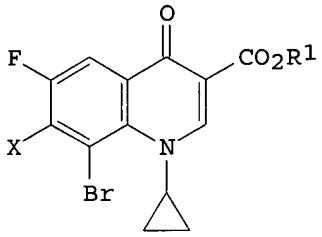
PRIORITY APPLN. INFO.: JP 1985-200240 19850910
OTHER SOURCE(S): MARPAT 107:58883
GI



I



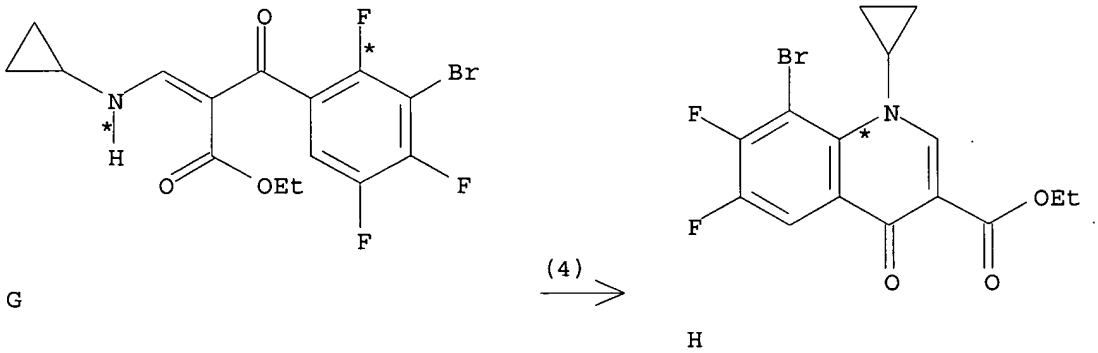
II



IV

AB The title compds. (I; R1-R4 = H, alkyl), effective antibacterials, are prepared Heating a mixture of Et (3-bromo-2,4,5-trifluorobenzoyl)acetate 1.5, HC(OEt)3 1.0, and Ac2O 1.2 g at 130° gave 1.75 g benzoylacrylate II (R5 = EtO), which was stirred with 3.32 g cyclopropylamine in EtOH at 5-20° to give 1.36 g II (R5 = cyclopropylamino) (III). Heating 1.35 g III with 0.23 g NaF in DMF at 108° gave 1.05 g quinoline IV (R1 = Et, X = F), which was hydrolyzed with HOAc and dilute H2SO4 to give 0.28 g IV (R1 = H, X = F) (V). Heating 0.2 g V with 0.2 g piperazine in Me2SO at 65-78° gave 20 mg I (R1-R4 = H), which was converted to its HCl salt, which had a min. inhibitory concentration of 0.05 μg/mL against Bacillus subtilis.

RX(4) OF 12 ...G ===> H...



G

H

RX(4) RCT G 104222-48-2
PRO H 104222-49-3

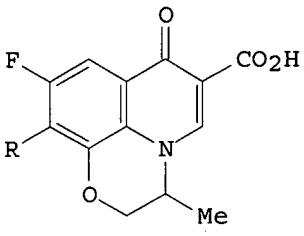
L7 ANSWER 60 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 107:39724 CASREACT
TITLE: Pyridonecarboxylic acids as antibacterial agents.

Part 6. A new synthesis of 7H-pyrido[1,2,3-de][1,4]benzoxazine derivatives including an antibacterial agent, ofloxacin

AUTHOR(S): Egawa, Hiroshi; Miyamoto, Teruyuki; Matsumoto, Junichi
CORPORATE SOURCE: Res. Lab, Dainippon Pharm. Co., Ltd., Suita, 564, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (1986), 34(10), 4098-102
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English

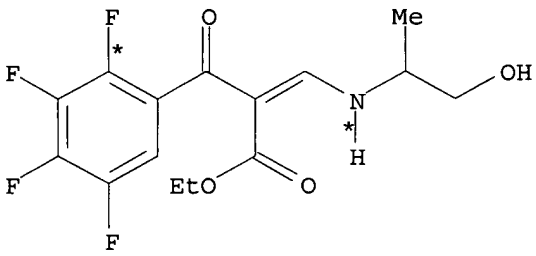
GI



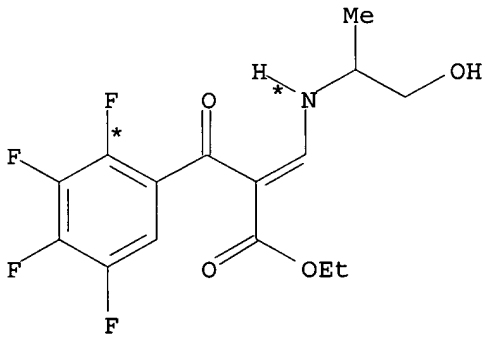
I

AB A new method for the synthesis of 7H-pyrido[1,2,3-de][1,4]benzoxazine derivs. I (R = F, 4-methyl-1-piperazinyl) was developed. The method is characterized by the intramol. cyclization of 1-(1-hydroxyprop-2-yl)-8-fluoro-4-quinolones which are prepared in three or four steps from Et 2,3,4,5-tetrafluorobenzoylacetate.

RX(2) OF 31 ...D + E ===> 2 G...

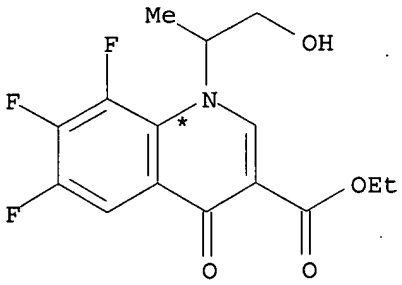


D

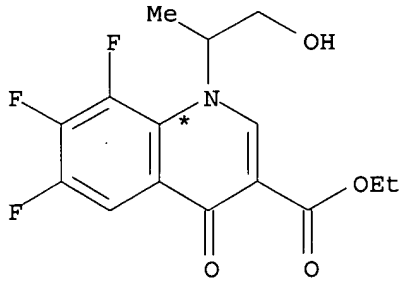


E

(2)



G
YIELD 32%



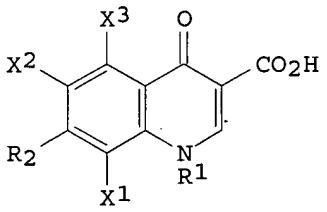
G
YIELD 32%

RX(2) RCT D 108943-39-1, E 108943-41-5
RGT H 865-47-4 t-BuOK
PRO G 107359-16-0
SOL 109-99-9 THF

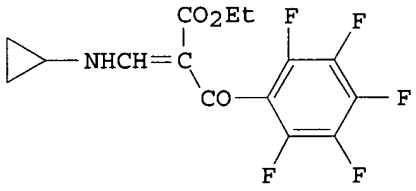
L7 ANSWER 61 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:213777 CASREACT
TITLE: Quinolone and quinolonecarboxylate esters and salts as antibacterials
INVENTOR(S): Matsumoto, Junichi; Miyamoto, Koshi; Egawa, Hiroshi; Nakamura, Shinichi
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62000469	A	19870106	JP 1985-141249	19850627

PRIORITY APPLN. INFO.: JP 1985-141249 19850627
GI



I

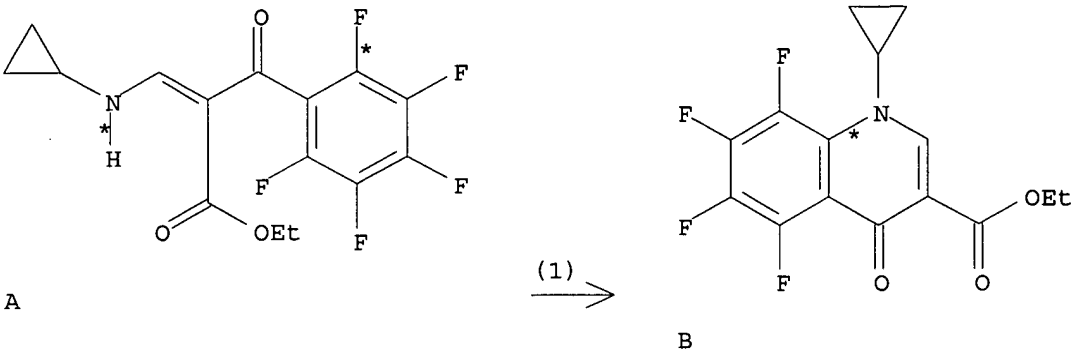


II

AB Title compds. I (R1 = alkyl, cycloalkyl, aryl; R2 = halo, OH, alkoxy, aryloxy, etc.; X1, X2, X3 = halo), useful as bactericides, are prepared A solution of II (preparation given) in THF was treated with NaH to give I (R1 = cyclopropyl; R2 = X1 = X2 = X3 = F) Et ester, which was hydrolyzed with H2SO4 and AcOH to afford I. I.HCl (R1 = cyclopropyl; R2 =

β-aminomethyl-1-pyrrolidinyl; X1 = X2 = X3 = F) (III) at 0.025 μg/mL proved effective against S. (Staphylococcus) aureusand S. pyogenes.

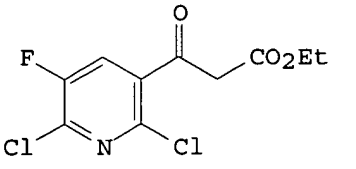
RX(1) OF 3 A ===> B...



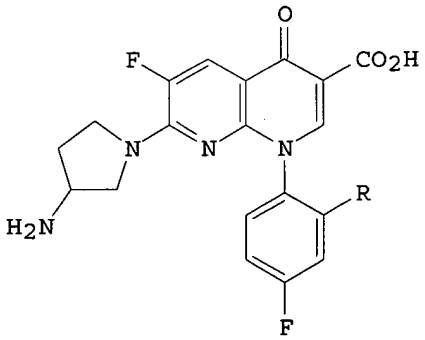
A B

RX(1) RCT A 107564-01-2
PRO B 107564-02-3

L7 ANSWER 62 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:196291 CASREACT
TITLE: Pyridonecarboxylic acids as antibacterial agents. V. Synthesis and structure-activity relationship of 7-amino-6-fluoro-1-(fluorophenyl)-4-oxo-1,8-naphthyridine-3-carboxylic acids
AUTHOR(S): Narita, Hirokazu; Konishi, Yoshinori; Nitta, Jun; Kitayama, Isao; Miyazima, Mikako; Watanabe, Yasuo; Yotsuji, Akira; Saikawa, Isamu
CORPORATE SOURCE: Res. Lab., Toyama Chem. Co., Ltd., Toyama, 930, Japan
SOURCE: Yakugaku Zasshi (1986), 106(9), 802-7
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



I

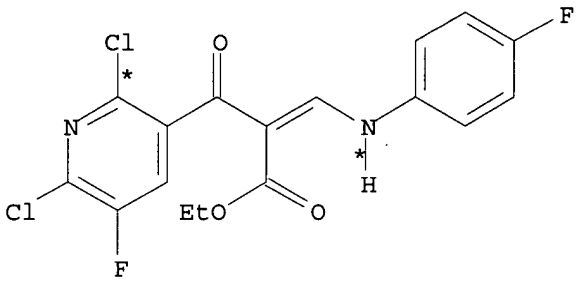


II

AB A series of 7-amino derivs. (unsubstituted and substituted piperazine,

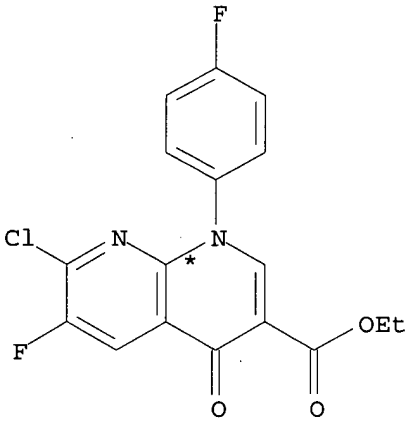
pyrrolidine and piperidine) of 1-aryl-6-fluoro-4-oxo-1,8-naphthyridine-3-carboxylic acid (aryl = 4-fluoro-, 2,4-difluoro- and 3,4-difluorophenyl) has been prepared starting from pyridine I, and their antibacterial activity and urinary recovery in mice were evaluated. Thus, (aminopyrrolidinyl)naphthyridinecarboxylic acids II (R = H, F) showed excellent activity against S. aureus (min. inhibitory concentration <0.05 μg/mL) as well as gram-neg. bacteria. A structure-activity relationship concerning 7-amino groups is also discussed.

RX(5) OF 84 ...F ===> L...



F

(5) →

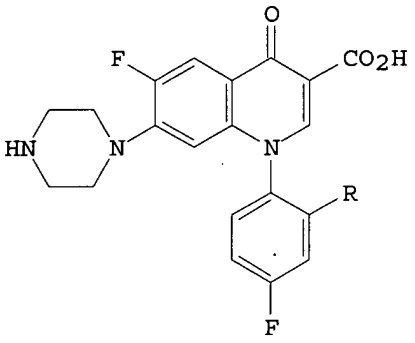


L

RX(5) RCT F 100491-00-7
RGT M 144-55-8 NaHCO3
PRO L 100491-30-3
SOL 68-12-2 DMF

L7 ANSWER 63 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:196218 CASREACT
TITLE: Pyridonecarboxylic acids as antibacterial agents. IV. Synthesis and structure-activity relationship of 7-amino-1-aryl-6-fluoro-4-quinolone-3-carboxylic acids
AUTHOR(S): Narita, Hirokazu; Konishi, Yoshinori; Nitta, Jun;

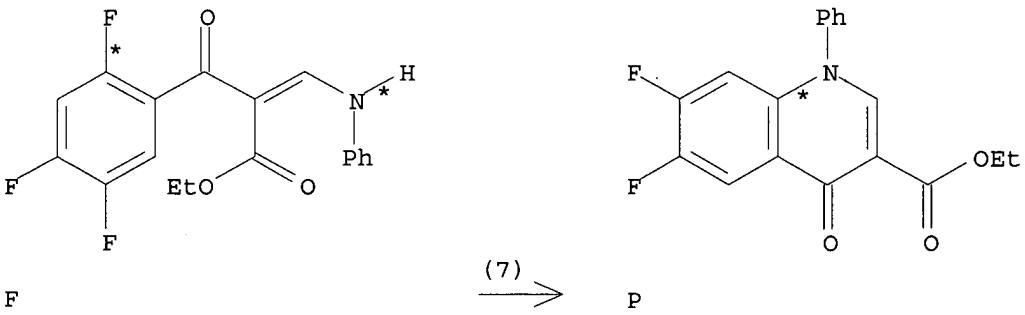
Nagaki, Hideyoshi; Kobayashi, Yoriko; Watanabe, Yasuo; Minami, Shinzaburo; Saikawa, Isamu
CORPORATE SOURCE: Res. Lab., Toyama Chem. Co., Ltd., Toyama, 930, Japan
SOURCE: Yakugaku Zasshi (1986), 106(9), 795-801
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



I

AB A series of unsubstituted and substituted cyclic amino derivs. at the 7-position of 1-aryl-6-fluoro-4-quinolone-3-carboxylic acid has been prepared starting from 2,4,5-F3C6H2COCH2CO2Et. The piperazino derivs. I (R = H, F) showed better in vitro activity than norfloxacin and good urinary recovery. 7-(3-Methyl-1-piperazinyl) and 7-(3-amino-1-pyrrolidinyl) derivs. of 1-(2,4-difluorophenyl)-6-fluoro-4-quinolone-3-carboxylic acids exhibited comparable in vitro activity and excellent in vivo efficacy on systemic infections and practically no toxicity. A structure-activity relationship focused on 7-substituents is also discussed.

RX(7) OF 114 ...F ===> P...



F P

RX(7) RCT F 108115-65-7
RGT Q 584-08-7 K2CO3
PRO P 108138-15-4
SOL 68-12-2 DMF

L7 ANSWER 64 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:102061 CASREACT

TITLE: Synthesis and structure-activity relationship of 1-aryl-6,8-difluoroquinolone antibacterial agents

AUTHOR(S): Chu, Daniel T. W.; Fernandes, Prabhavathi B.; Maleczka, Robert E., Jr.; Nordeen, Carl W.; Pernet, Andre G.

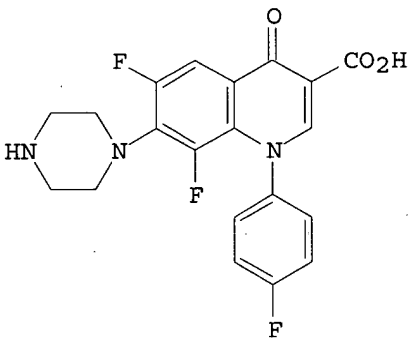
CORPORATE SOURCE: Anti-Infect. Res. Div., Abbott Lab., Abbott Park, IL, 60064, USA

SOURCE: Journal of Medicinal Chemistry (1987), 30(3), 504-9
CODEN: JMCMAR; ISSN: 0022-2623

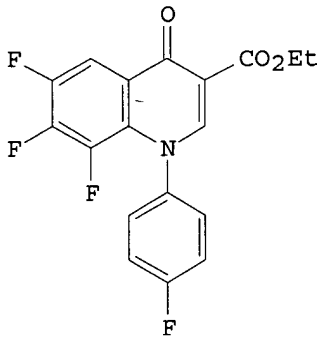
DOCUMENT TYPE: Journal

LANGUAGE: English

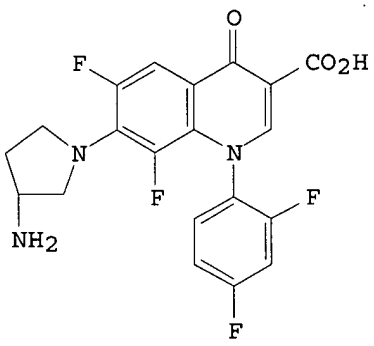
GI



I



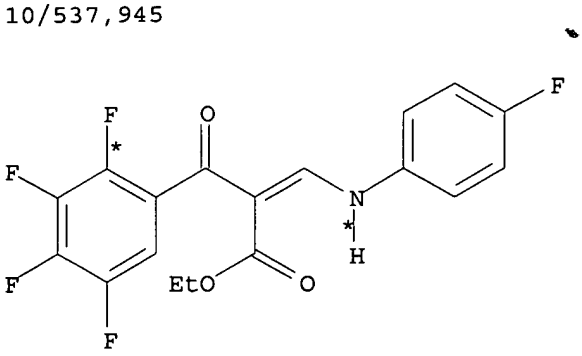
II



III

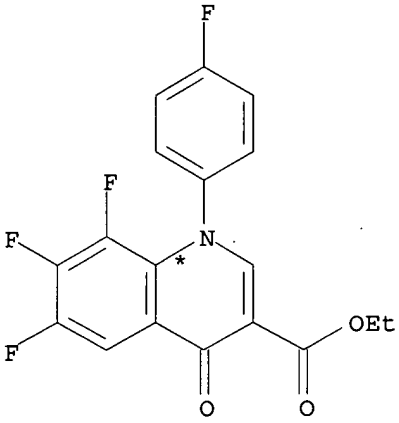
AB New arylfluoroquinolones, e.g., I, were prepared that have F atoms at the 6- and 8-positions, substituted amino groups at the 7-position, and substituted Ph groups at the 1-position. Thus, RCOCH2CO2Et (R = 2,3,4,5-tetrafluorophenyl) was treated with CH(COEt)3 and Ac2O, followed by 4-FC6H4NH2 in CH2Cl2, to give 87% RCOC(:CHNHR1)CO2Et (R1 = 4-FC6H4), which underwent intramol. cyclocondensation when treated with NaH in THF to give 71% quinolone ester II. Hydrolyzing II with NaOH in THF, and then treatment with piperazine in pyridine gave I. Arylfluoroquinolones, e.g., III, in which the 1-substituent is 2,4-difluorophenyl and the 7-substituent is a 3-amino-1-pyrrolidinyl group, have the greatest in vitro antibacterial potency. I was also found to possess excellent in vitro potency and in vivo efficacy.

RX(6) OF 90 ...F ===> S...



F

(6)



S
YIELD 71%

RX(6) RCT F 105859-07-2

STAGE(1)
RGT R 7646-69-7 NaH
SOL 109-99-9 THF, 7727-37-9 N2

STAGE(2)
RGT T 64-19-7 AcOH

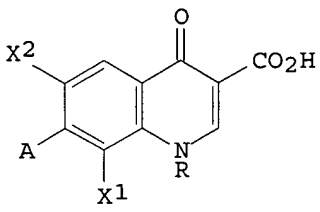
PRO S 105859-09-4

L7 ANSWER 65 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:84650 CASREACT
TITLE: 1-Aryl-4-quinolone-3-carboxylic acids, their preparation, and their use as antibacterials and feed additives
INVENTOR(S): Grohe, Klaus; Zeiler, Hans Joachim; Metzger, Karl
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 87 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3517535	A1	19861120	DE 1985-3517535	19850515
EP 201829	A1	19861120	EP 1986-106115	19860505
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
EP 318468	A1	19890531	EP 1989-100850	19860505
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
JP 61263959	A	19861121	JP 1986-107801	19860513
US 4980353	A	19901225	US 1986-862863	19860513
US 4981854	A	19910101	US 1989-431943	19891106
PRIORITY APPLN. INFO.:			DE 1985-3517535	19850515
			EP 1986-106115	19860505
			US 1986-862863	19860513
			US 1988-239151	19880831

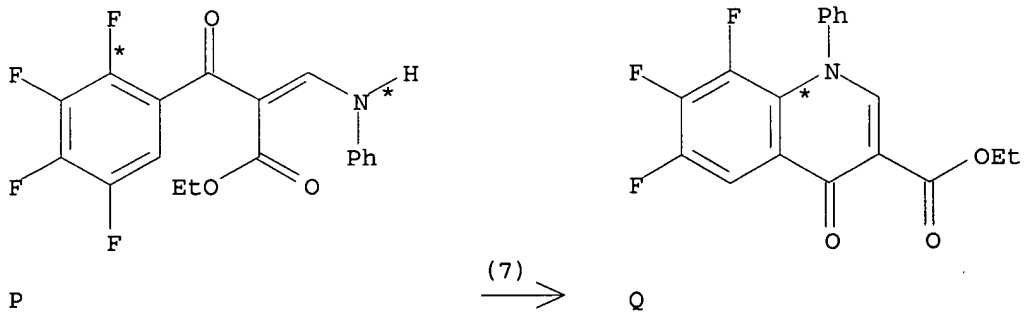
OTHER SOURCE(S): MARPAT 106:84650
GI



I

AB (Cyclic amino)quinolones I [X1 = halo, NO2; X2 = halo; R = (un)substituted Ph, heteroaryl with O, S, or N atoms; A = halo, (un)substituted 1-piperazinyl, 1-pyrrolidinyl] and their pharmaceutically useable hydrates, salts, etc., useful as antibacterials and feed additives, were prepared by 3 methods. 2,3,4,5-F4C6HCOC(:CHOEt)CO2Et in EtOH was treated with 4-FC6H4NH2 to give 2,3,4,5-F4C6HCOC(:CHNHC6H4F-4)CO2Et which was cyclized with NaF in DMF to give I (X1 = X2 = A = F, R = 4-FC6H4) (II) as its Et ester. This was hydrolyzed with aqueous AcOH-H2SO4 to give II. Refluxing II with piperazine gave I (X1 = X2 = F, R = 4-FC6H4, A = 1-piperazinyl) (III). The min. inhibitory concentration (MIC) of III for Escherichia coli 4418 was 0.25 μg/mL. The MIC for 10 other bacterial strains were also obtained. A formulation for coated tablets was given.

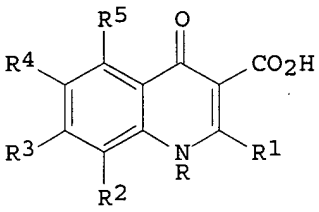
RX(7) OF 58 ...P ===> Q...



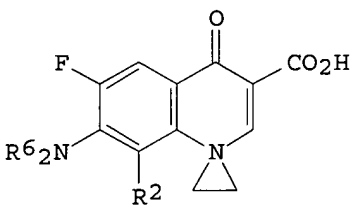
P (7) Q

RX(7) RCT P 106809-20-5
PRO Q 104599-93-1
CAT 148116-22-7 Pyrido[1,2-a][1,4]diazepine, 3,4,5,7,8,9,10,10a-octahydro-

L7 ANSWER 66 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:84368 CASREACT
TITLE: Cycloaracylation of enamines. I. Synthesis of 4-quinolone-3-carboxylic acids
AUTHOR(S): Grohe, Klaus; Heitzer, Helmut
CORPORATE SOURCE: Wiss. Hauptlab., Bayer A.-G., Leverkusen, D-5090, Fed. Rep. Ger.
SOURCE: Liebigs Annalen der Chemie (1987), (1), 29-37
CODEN: LACHDL; ISSN: 0170-2041
DOCUMENT TYPE: Journal
LANGUAGE: German
GI



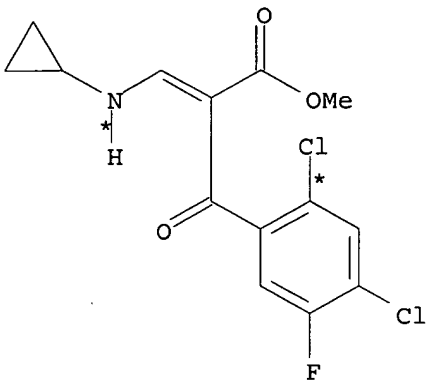
I



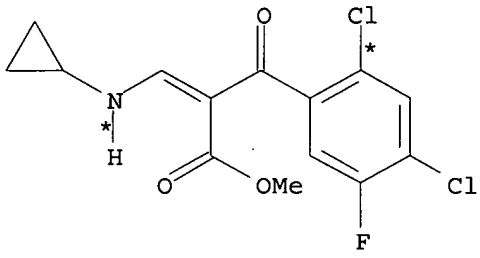
II

AB Quinolinecarboxylic acids I (R = cyclopropyl, Ph, Et; R1 = H, Me; R2 = H, F, NO2; R3 = H, Cl, F, NO2; R4 = F, Cl, H; R5 = H, Cl) were prepared from 2,3,4,5,6-R6R2R3R4R5C6COCl (R6 = Cl, F, NO2, MeO, MeS) and enamines or CH2(CO2Et)2. Thus, 2,4,5-Cl2(O2N)C6H2COCl was treated with RNHCH:CHCO2Me (R = cyclopropyl) to give 2,4,5-Cl2(O2N)C6H2COC(CO2Me):CHNHR, which was cyclized by Me3COK and the product hydrolyzed to give I (R = cyclopropyl, R1 = R2 = R5 = H, R3 = Cl, R4 = NO2). The antibacterial aminoquinoline derivs. II (R2 = H, F, NO2, R62N = piperazine 4-methyl-, 4-ethyl-, 4-(hydroxyethyl)piperazino, pyrrolidino, piperidino) were prepared from the corresponding I (R3 = halo).

RX(31) OF 401 ...U + V ===> 2 CT...

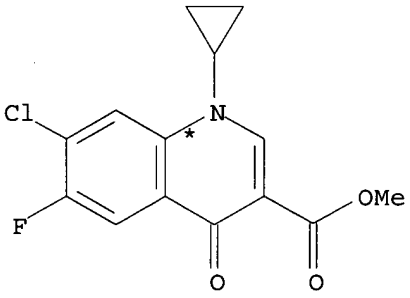


U

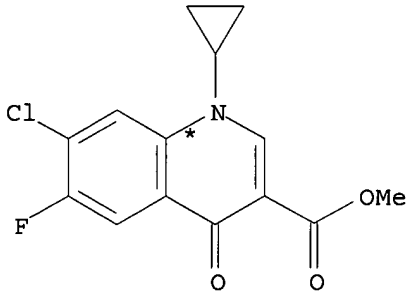


V

(31)



CT

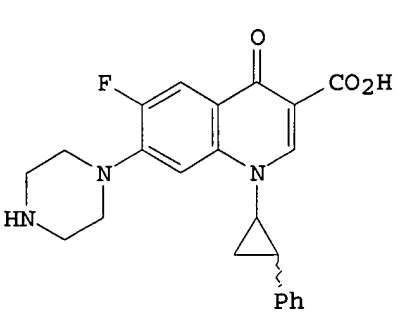


CT

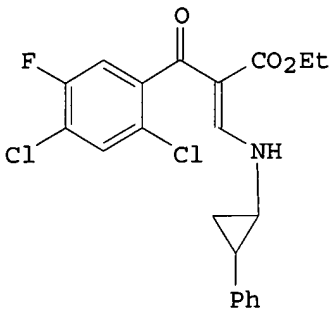
RX(31) RCT U 104600-21-7, V 104600-25-1
RGT CU 584-08-7 K2CO3
PRO CT 104599-90-8
SOL 68-12-2 DMF

L7 ANSWER 67 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:84360 CASREACT
TITLE: Chiral DNA gyrase inhibitors. 1. Synthesis and antimicrobial activity of the enantiomers of 6-fluoro-7-(1-piperazinyl)-1-(2-trans-phenylcyclopropyl)-1,4-dihydro-4-oxoquinoline-3-carboxylic acid
AUTHOR(S): Mitscher, Lester A.; Sharma, Padam N.; Chu, Daniel T. W.; Shen, Linus L.; Pernet, Andre G.
CORPORATE SOURCE: Dep. Med. Chem., Kansas Univ., Lawrence, KS, 66045, USA
SOURCE: Journal of Medicinal Chemistry (1986), 29(10), 2044-7
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal
LANGUAGE: English
GI



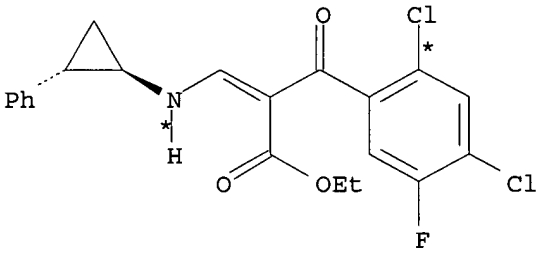
I



II

AB New quinoline antimicrobial agents [racemic-, (1'S,2'R)-, and (1'R,2'S)-6-fluoro-7-(1-piperazinyl)-1-(2'-trans-phenyl-1'-cyclopropyl)-1,4-dihydro-4-oxoquinoline-3-carboxylic acid [(1'R,2'S)-I]] were prepared from 2,4,5-Cl2FC6H2COCH2CO2Et via cyclization of unsatd. esters II, and their in vitro antimicrobial potencies and spectra were determined As compared to their conceptual parents, these agents retained a considerable amount of the antimicrobial potency and spectra of ciprofloxacin and of 6-fluoro-1-phenyl-7-(1-piperazinyl)-1,4-dihydro-4-oxoquinoline-3-carboxylic acid against gram-positives. Gram-negs. were considerably less sensitive. (-)-(1'-S,2'-R)-I was the more potent of the enantiomers, but the degree of chiral discrimination by most bacteria was only 4-fold.

RX(3) OF 61 ...F ===> H...



F

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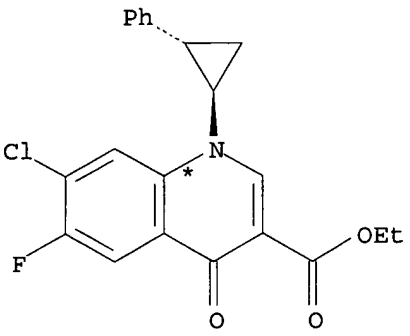


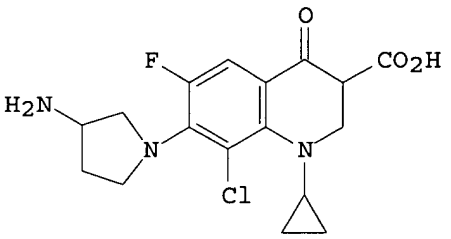
H

RX(3) RCT F 103477-53-8
RGT I 7646-69-7 NaH
PRO H 103477-54-9
SOL 109-99-9 THF

L7 ANSWER 68 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:50068 CASREACT
TITLE: Quinolonecarboxylic acid derivatives
INVENTOR(S): Irikura, Tsutomu; Suzue, Seigo; Murayama, Satoshi; Hirai, Keiji; Ishizaki, Takayoshi
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 195316	A1	19860924	EP 1986-102938	19860306
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 61205258	A	19860911	JP 1985-46216	19850308
JP 61225181	A	19861006	JP 1986-22296	19860204
JP 05064955	B	19930916		
AU 8654272	A	19860911	AU 1986-54272	19860304
HU 40639	A2	19870128	HU 1986-888	19860304
FI 8600950	A	19860909	FI 1986-950	19860306
FI 85698	B	19920214		
FI 85698	C	19920525		
DK 8601039	A	19860909	DK 1986-1039	19860307
DK 161383	B	19910701		
DK 161383	C	19911209		
NO 8600870	A	19860909	NO 1986-870	19860307
NO 165071	B	19900910		
NO 165071	C	19901219		
CN 86102363	A	19870121	CN 1986-102363	19860307
CN 1012613	B	19910515		
ES 552802	A1	19870416	ES 1986-552802	19860307
PRIORITY APPLN. INFO.:			JP 1985-46216	19850308
			JP 1986-22296	19860204

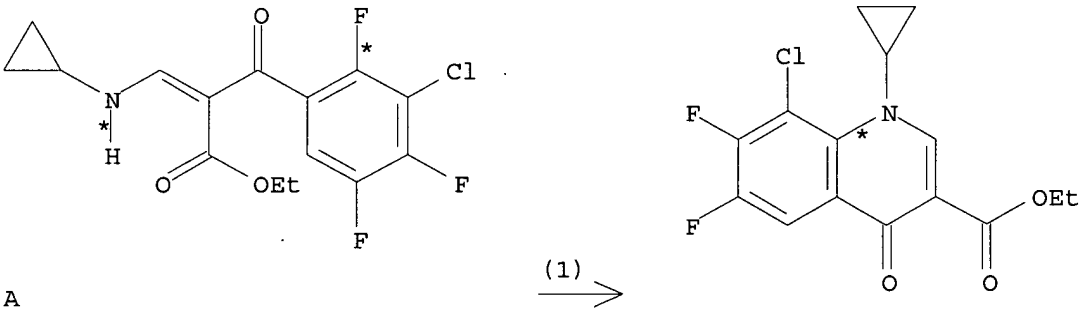
GI



I

AB Quinolonecarboxylic acid I, useful as an antibacterial agent, was prepared Thus, 7-[3-(tert-butoxycarbonylamino)-1-pyrrolidinyl]-8-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid, prepared in 17 steps from 3,4-ClFC6H4NH2, was deprotected to give I. In vivo antibacterial activity against systemic infections in mice I was very effective against Streptococcus pneumoniae, on which the reference compds. were ineffective.

RX(1) OF 7 A ===> B...



A

B

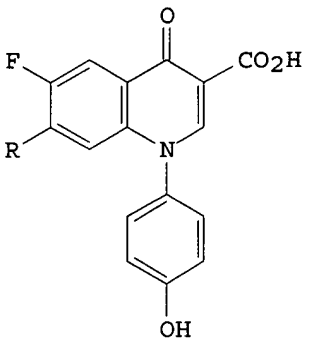
RX(1) RCT A 101987-88-6
PRO B 99696-21-6

L7 ANSWER 69 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:32843 CASREACT
TITLE: Quinolone derivatives
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

JP 61122273	A	19860610	JP 1985-256309	19851114
PRIORITY APPLN. INFO.:			GB 1984-29142	19841119

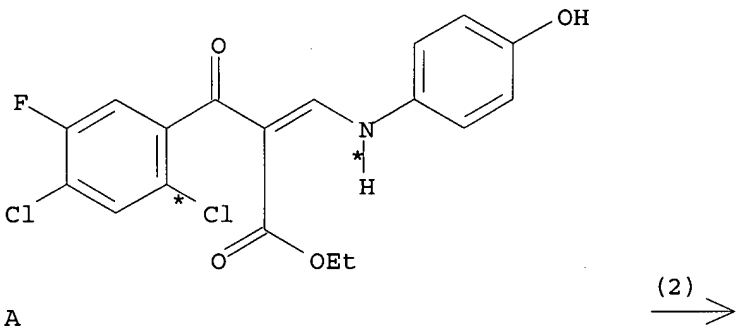
GI



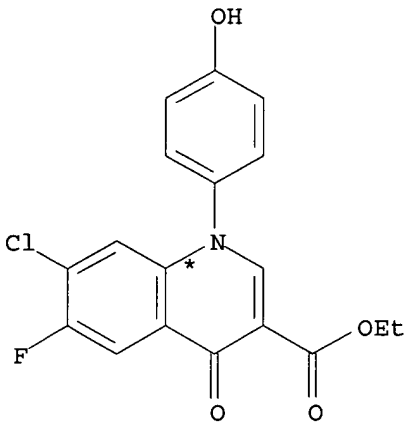
I

AB The title compds. (I; R = chloro, 1-pyrrolidinyl, piperidino, N-methylbenzylamino, methylamino, or dimethylamino) are prepared as bactericides. Thus, 1-(4-hydroxyphenyl)-3-ethoxycarbonyl-6-fluoro-7-chloro-4-quinolone was treated with pyrrolidine to give I (R = 1-pyrrolidinyl). The min. inhibitory concns. of this product against Staphylococcus aureus and Streptococcus faecalis in culture media were 0.050 and 0.780 μg/mL, resp.

RX(2) OF 2 A ===> C



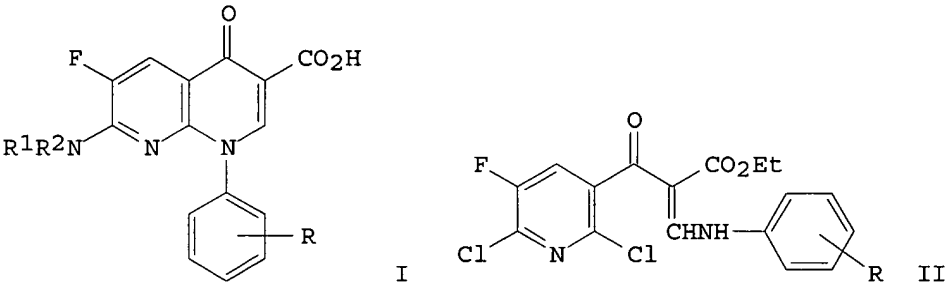
A



C

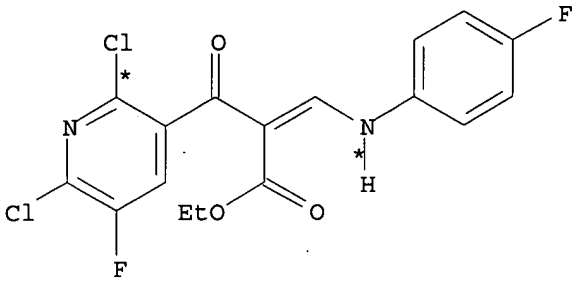
RX(2) RCT A 98105-67-0
PRO C 98105-86-3

L7 ANSWER 70 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:18399 CASREACT
TITLE: Synthesis and structure-activity relationships of new arylfluoronaphthyridine antibacterial agents
AUTHOR(S): Chu, Daniel T. W.; Fernandes, Prabhavathi B.; Claiborne, Akiyo K.; Gracey, Eugene H.; Pernet, Andre G.
CORPORATE SOURCE: Anti-infect. Res. Div., Abbott Lab., North Chicago, IL, 60064, USA
SOURCE: Journal of Medicinal Chemistry (1986), 29(11), 2363-9
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



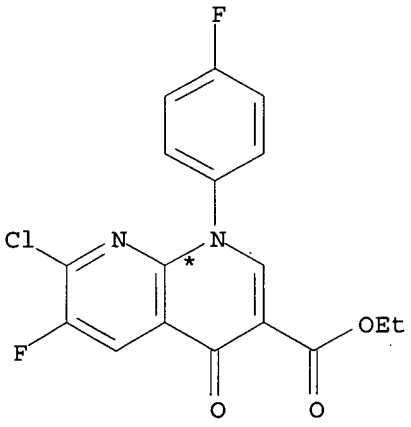
AB The aminonaphthyridinecarboxylic acids I (R = H, 4-F, 2,4-F2, R1R2N = piperazino, 3-hydroxypyrrolidino, 3- and 4-methylpiperazino, 3-aminopyrrolidino) were prepared from Et 2,6-dichloro-5-fluoro-3-pyridinecarboxylate via cyclization of the esters II. The in vitro antibacterial activity is greatest for I (R = 4-F, 2,4-F2; R1R2N = 3-aminopyrrolidino).

RX(7) OF 163 ...O ===> T...



O

(7)



T

RX(7) RCT O 100491-00-7
RGT U 7646-69-7 NaH
PRO T 100491-30-3
SOL 109-99-9 THF

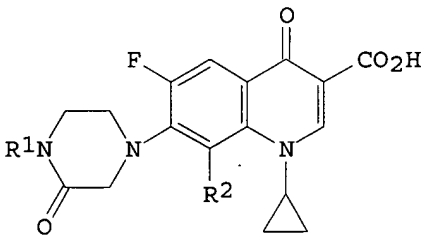
=> d ibib abs fhit 71-80

L7 ANSWER 71 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:18376 CASREACT
TITLE: Antibacterial 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(3-oxo-1-piperazinyl)-3-quinolinecarboxylic acids
INVENTOR(S): Petersen, Uwe; Grohe, Klaus; Zeiler, Hans Joachim; Metzger, Karl
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 30 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3420770	A1	19851205	DE 1984-3420770	19840604
US 4588726	A	19860513	US 1985-735499	19850517
EP 166939	A1	19860108	EP 1985-106254	19850522
EP 166939	B1	19880622		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
AT 35264	T	19880715	AT 1985-106254	19850522
JP 61001682	A	19860107	JP 1985-116835	19850531
IL 75367	A	19880930	IL 1985-75367	19850531
CA 1248953	A1	19890117	CA 1985-482910	19850531
DK 8502493	A	19851205	DK 1985-2493	19850603
ZA 8504164	A	19860129	ZA 1985-4164	19850603
ES 543837	A1	19860601	ES 1985-543837	19850603
CA 1259315	A2	19890912	CA 1988-577424	19880914
PRIORITY APPLN. INFO.:			DE 1984-3420770	19840604
			EP 1985-106254	19850522
			CA 1985-482912	19850531

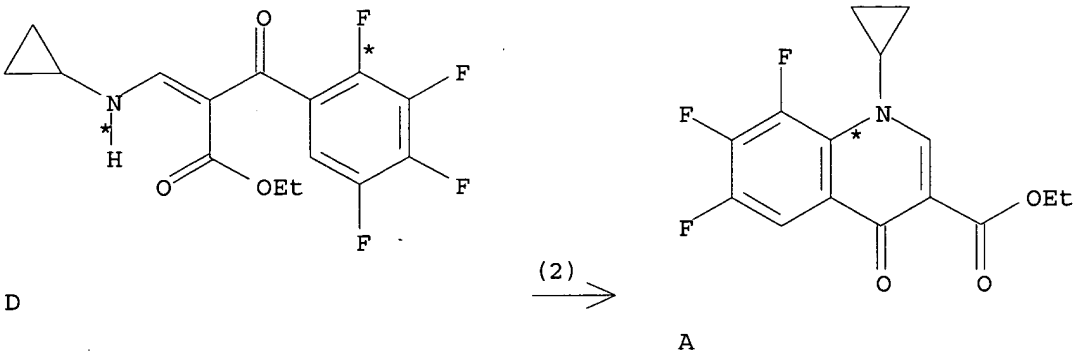
OTHER SOURCE(S): MARPAT 106:18376
GI



I

AB Title compds. I (R1 = H, Me, Et; R2 = H, F), their hydrates, and alkali and alkaline earth metal salts, useful as antibacterials, are prepared Thus, 1-cyclopropyl-6,7-difluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid was treated with 2-piperazinone to give I (R1 = R2 = H). A lacquer-coated tablet contained I (R1 = H, R2 = F) 291.5, microcryst. cellulose 27.5, corn starch 36.0, poly(1-vinyl-2-pyrrolidone) 15.0, SiO2 2.5, and Mg stearate 2.5 mg.

RX(2) OF 9 D ===> A...



D

A

RX(2) RCT D 94695-51-9
PRO A 94242-51-0

L7 ANSWER 72 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 106:4900 CASREACT
TITLE: 7-Amino-1-cyclopropyl-1,4-dihydro-4-oxo-3-quinolinecarboxylates and their bactericidal use and formulation
INVENTOR(S): Schriewer, Michael; Grohe, Klaus; Zeiler, Hans Joachim; Metzger, Karl Georg
PATENT ASSIGNEE(S): Bayer A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 72 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3509546	A1	19860925	DE 1985-3509546	19850316
US 4705788	A	19871110	US 1986-834170	19860227
EP 198192	A1	19861022	EP 1986-102769	19860303
EP 198192	B1	19920513		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
EP 300155	A2	19890125	EP 1988-107985	19860303
EP 300155	A3	19900117		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
AT 76074	T	19920515	AT 1986-102769	19860303
JP 61218575	A	19860929	JP 1986-56105	19860315
JP 05060827	B	19930903		
JP 05213836	A	19930824	JP 1992-194644	19920630
JP 2504895	B2	19960605		

PRIORITY APPLN. INFO.: DE 1985-3509546 19850316
EP 1986-102769 19860303
OTHER SOURCE(S): MARPAT 106:4900
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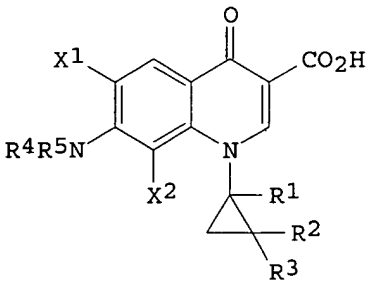
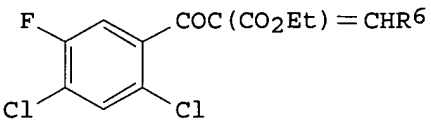


I



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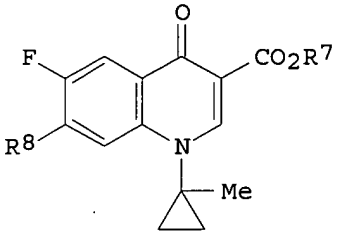
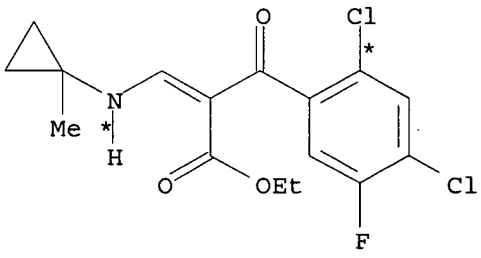


III

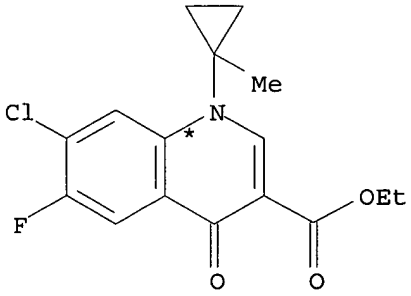
AB Title compds. [I; X1, X2 = H, halo; R1-R3 = H, Me, Cl, F; R4R5N = (un)substituted 5- or 6-membered heterocyclyl] were prepared Thus, benzoylacrylate II (R6 = OEt) reacted with 1-amino-1-methylcyclopropane to give II (R6 = 1-methylcyclopropylamino), which cyclized to give quinolinecarboxylate III (R7 = Et, R8 = Cl). This was hydrolyzed to give III (R7 = H, R8 = Cl) which was treated with piperazine to form III (R7 = H, R8 = 1-piperazinyl) (IV). IV was bactericidal against Escherichia coli and Klebsiella. IV was formulated into tablets containing IV 583.0, cellulose 55.0, corn starch 72.0, insol. polyvinylpyrrolidone 30.0, SiO2 5.0, and Mg stearate 5.0 mg, which were coated.

RX(2) OF 6 ...C ===> D...



C

(2)



D

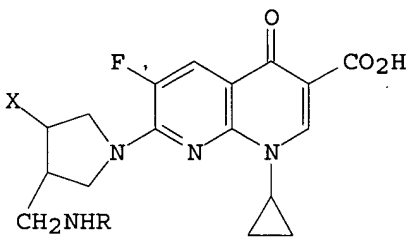
RX(2) RCT C 105614-20-8
PRO D 105614-21-9
CAT 584-08-7 K2CO3

L7 ANSWER 73 OF 103 CASREACT COPYRIGHT 2006 ACS on STN

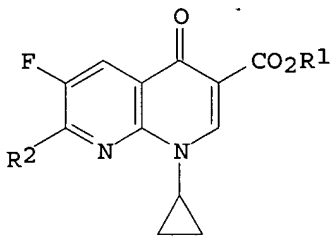
ACCESSION NUMBER: 105:226521 CASREACT
TITLE: 1,8-Naphthyridine derivatives
INVENTOR(S): Matsumoto, Junichi; Nakano, Junji; Chiba, Katsumi; Nakamura, Shinichi
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 48 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 191451	A1	19860820	EP 1986-101681	19860210
EP 191451	B1	19890802		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 61189281	A	19860822	JP 1985-28998	19850215
JP 06035458	B	19940511		
JP 61243081	A	19861029	JP 1985-84985	19850419
AU 8653216	A	19860821	AU 1986-53216	19860205
AU 578793	B2	19881103		
FI 8600556	A	19860816	FI 1986-556	19860207
US 4738968	A	19880419	US 1986-829097	19860212
ZA 8601074	A	19860924	ZA 1986-1074	19860213
DK 8600717	A	19860816	DK 1986-717	19860214
HU 41784	A2	19870528	HU 1986-644	19860214
ES 552032	A1	19870601	ES 1986-552032	19860214
SU 1456015	A3	19890130	SU 1986-4023809	19860214
PRIORITY APPLN. INFO.:			JP 1985-28998	19850215
			JP 1985-84985	19850419

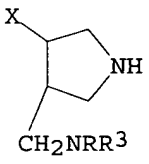
OTHER SOURCE(S): MARPAT 105:226521
GI



I



II

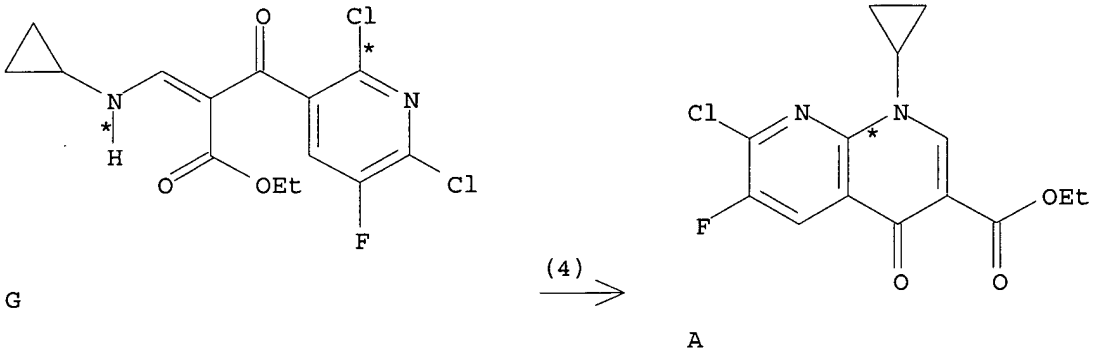


III

AB Bactericidal pyrrolidinonaphthyridines I (X = F, Cl; R = H, Me, Et) and their esters are by treating naphthyridines II (R1 = H, aliphatic; R2 = reactive group replaceable by N) with pyrrolidines III (R3 = H, protective group). Thus, II (R1 = H, R2 = Cl) (IV) was prepared in 6 steps from 2,6-dichloro-5-fluoronicotinonitrile, and cis-III (X = Cl, R = H, R1 = Ac)

(V) was prepared in 5 steps from 1-benzyl-3-hydroxy-4-(hydroxymethyl)pyrrolidine. IV reacted with V to give cis-I (X = Cl, R = OAc), which was hydrolyzed with HCl to give cis-I (X = Cl, R = H) (VI). VI was active against gram-pos. and gram-neg. bacteria in vitro, and had an ED50 of 0.355 mg/kg i.v. against Staphylococcus aureus and 0.235 mg/kg i.v. against Streptococcus pyogenes in mice. Capsules containing VI.HCl 250, starch 50, lactose 35, and talc 15 mg were prepared

RX(4) OF 21 ...G ===> A...



G

A

RX(4) RCT G 96568-06-8
PRO A 96568-07-9

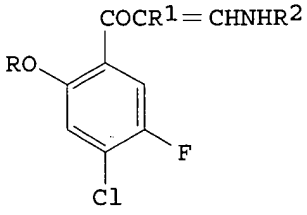
L7 ANSWER 74 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 105:225803 CASREACT
TITLE: 3-Aminoacrylic acid derivatives
INVENTOR(S): Maurer, Fritz; Grohe, Klaus
PATENT ASSIGNEE(S): Bayer A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 42 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3501247	A1	19860717	DE 1985-3501247	19850116
EP 188194	A2	19860723	EP 1986-100052	19860103
EP 188194	A3	19870826		
EP 188194	B1	19900704		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
AT 54306	T	19900715	AT 1986-100052	19860103
US 4695646	A	19870922	US 1986-816544	19860106
JP 61167639	A	19860729	JP 1986-3717	19860113
IL 77575	A	19881230	IL 1986-77575	19860113
FI 8600167	A	19860717	FI 1986-167	19860114
DD 242222	A5	19870121	DD 1986-286189	19860114
DK 8600181	A	19860717	DK 1986-181	19860115
NO 8600121	A	19860717	NO 1986-121	19860115
ZA 8600293	A	19860924	ZA 1986-293	19860115
CN 86100221	A	19860716	CN 1986-100221	19860116

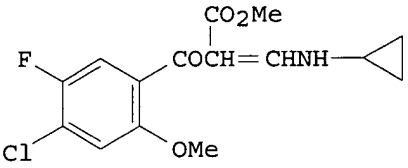
HU 40614	A2	19870128	HU 1986-225	19860116
HU 199400	B	19900228		
ES 550924	A1	19880701	ES 1986-550924	19860116
ES 550924	A5	19880728		
PRIORITY APPLN. INFO.:			DE 1985-3501247	19850116
			EP 1986-100052	19860103

OTHER SOURCE(S): MARPAT 105:225803

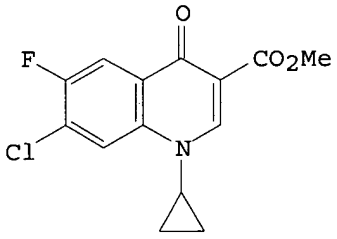
GI



I



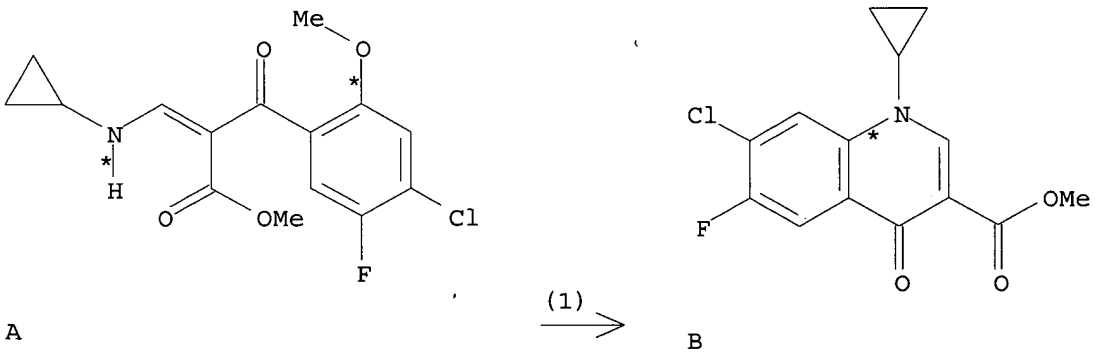
II



III

AB The title compds. I (R = alkyl; R1 = alkoxycarbonyl; R2 = alkyl, cycloalkyl, NH2, alkylamino, dialkylamino) were prepared as intermediates for oxoquinolinecarboxylic acid derivs. Aminoacrylate II was prepared in 5 steps from 3,4-ClFC6H3OH and AcCl in the presence of AlCl3. Cyclocondensation of II with K2CO3 in DMF in 2 h at .apprx.150° gave 66% quinoline III.

RX(1) OF 21 ...A ===> B



A

B

RX(1) RCT A 105533-65-1
PRO B 104599-90-8

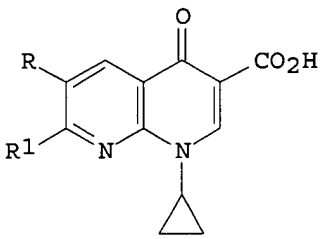
L7 ANSWER 75 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 105:191059 CASREACT
TITLE: 1-Cyclopropyl-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acids
INVENTOR(S): Petersen, Uwe; Grohe, Klaus; Zeiler, Hans Joachim; Metzger, Karl Georg
PATENT ASSIGNEE(S): Bayer A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 64 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3508816	A1	19860710	DE 1985-3508816	19850313
NO 8505134	A	19860711	NO 1985-5134	19851218
NO 163331	B	19900129		
NO 163331	C	19900509		
EP 187376	A2	19860716	EP 1985-116551	19851224
EP 187376	A3	19880504		
EP 187376	B1	19920513		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
AT 76076	T	19920515	AT 1985-116551	19851224
US 4840954	A	19890620	US 1985-815440	19851231
IL 77538	A	19920525	IL 1986-77538	19860107
FI 8600073	A	19860711	FI 1986-73	19860108
FI 86721	B	19920630		
FI 86721	C	19921012		
DD 241258	A5	19861203	DD 1986-286039	19860108
DD 257427	A5	19880615	DD 1986-296482	19860108
DD 257428	A5	19880615	DD 1986-296483	19860108
CA 1339373	C	19970826	CA 1986-499241	19860108
DK 8600091	A	19860711	DK 1986-91	19860109
DK 168439	B1	19940328		
JP 61161284	A	19860721	JP 1986-1485	19860109
JP 06053741	B	19940720		
ZA 8600163	A	19860924	ZA 1986-163	19860109
HU 40126	A2	19861128	HU 1986-87	19860109
HU 193623	B	19871130		
AU 8652164	A	19870122	AU 1986-52164	19860109
AU 574550	B2	19880707		
ES 550767	A1	19880616	ES 1986-550767	19860109
ES 550767	A5	19880715		
PL 148191	B1	19890930	PL 1986-264565	19860109
PL 148759	B1	19891130	PL 1986-257419	19860109
HU 202840	B	19910429	HU 1987-1847	19860109
CN 86100126	A	19860709	CN 1986-100126	19860110
CN 1003239	B	19890208		
NO 8600199	A	19860711	NO 1986-199	19860121
ES 557516	A1	19871016	ES 1987-557516	19870429
ES 557515	A1	19880216	ES 1987-557515	19870429
ES 557514	A1	19880301	ES 1987-557514	19870429
AU 8773118	A	19870910	AU 1987-73118	19870515
AU 576449	B2	19880825		
ES 557785	A1	19880416	ES 1987-557785	19871215
AU 8818359	A	19880915	AU 1988-18359	19880624

FI 8902675	A	19890601	FI 1989-2675	19890601
CA 1320206	C2	19930713	CA 1990-615694	19900405
PRIORITY APPLN. INFO.:			DE 1985-3500562	19850110
			DE 1985-3508816	19850313
			EP 1985-116551	19851224
			CA 1986-499241	19860108
			FI 1986-73	19860108

OTHER SOURCE(S): MARPAT 105:191059

GI



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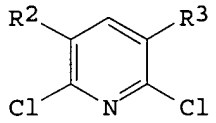
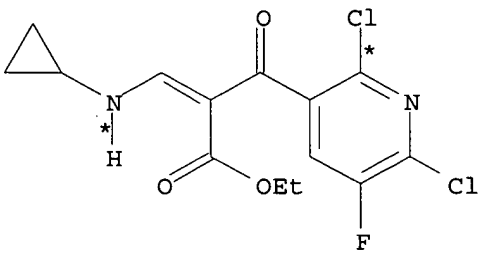


II

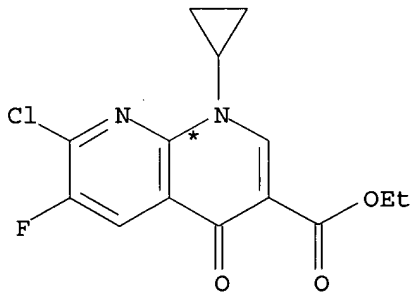
AB The title compds. [I; R = halo, NO2; R1 = (un)substituted 1-piperazinyl, 1-pyrrolidinyl] were prepared as bactericides and feed additives. Thus, 2,6-dichloro-5-methyl-3-pyridinamine (II, R2 = NH2, R3 = Me) was diazotized and coupled with Me2NH to give II (R2 = Me2NN:N, R3 = Me) which was fluorinated with HF to give II (R2 = F, R3 = Me). The latter was converted in 6 steps to II [R2 = F, R3 = EtO2CC(:CHOEt)CO] which was condensed with cyclopropylamine, followed by cyclization and hydrolysis of the ester group, to give I (R = F, R1 = Cl). The latter was heated with piperazine in Me2SO to give I (R = F, R1 = 1-piperazinyl) (III). III had a min. inhibitory concentration of ≤0.015 mcg/mL against Escherichia coli Neum. Tablets were prepared each containing III 583.0, microcyrst. cellulose 55.0, cornstarch 72.0, polyvinylpyrrolidine 30.0, dispersed silica 5.0, and Mg stearate 5.0 mg.

RX(1) OF 76 ...A ===> B...



A

(1)



B

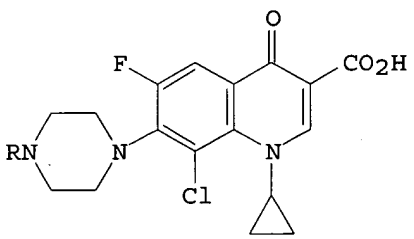
RX(1) RCT A 96568-06-8
PRO B 96568-07-9

CAT 584-08-7 K2CO3

L7 ANSWER 76 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 105:190961 CASREACT
TITLE: Quinolinecarboxylic acid derivatives
INVENTOR(S): Irikura, Tsutomu; Suzue, Seigo; Murayama, Satoshi; Hirai, Keiji; Ishizaki, Takayoshi
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: S. African, 26 pp.
CODEN: SFXXAB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ZA 8503954	A	19860129	ZA 1985-3954	19850524
JP 61205258	A	19860911	JP 1985-46216	19850308
HU 38337	A2	19860528	HU 1985-1962	19850523
HU 194865	B	19880328		
NO 8502076	A	19860909	NO 1985-2076	19850523
AU 8542829	A	19860911	AU 1985-42829	19850523
EP 195841	A1	19861001	EP 1985-106626	19850529
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
ES 543686	A1	19860401	ES 1985-543686	19850530
DK 8502415	A	19860909	DK 1985-2415	19850530
FI 8502172	A	19860909	FI 1985-2172	19850530
JP 61205238	A	19860911	JP 1985-118380	19850531
JP 04082138	B	19921225		
JP 61205237	A	19860911	JP 1985-118381	19850531
JP 07013041	B	19950215		
JP 61205239	A	19860911	JP 1985-118382	19850531
JP 05003866	B	19930118		
JP 61205235	A	19860911	JP 1985-118383	19850531
JP 61205240	A	19860911	JP 1985-118384	19850531
JP 61205259	A	19860911	JP 1985-118385	19850531
CN 85104693	A	19860903	CN 1985-104693	19850619
CN 1010779	B	19901212		

PRIORITY APPLN. INFO.: JP 1985-46216 19850308
OTHER SOURCE(S): MARPAT 105:190961
GI



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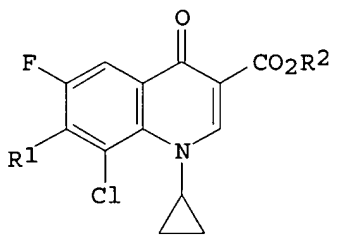
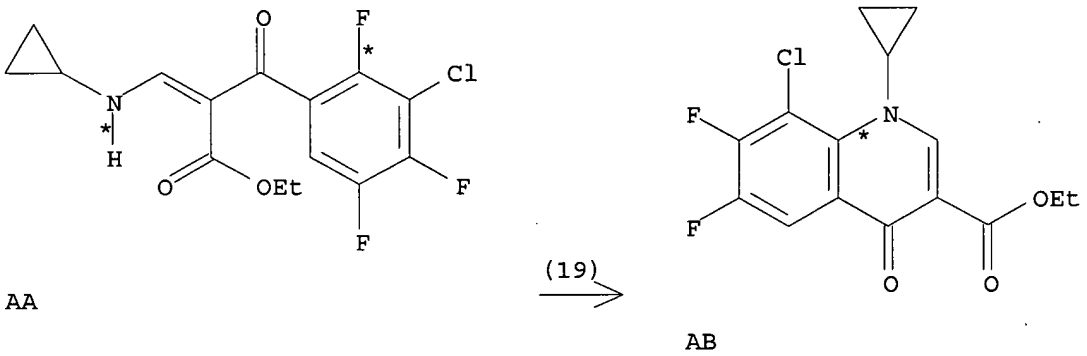


II

AB Title compds. I (R = H, Me), useful as bactericides, were prepared Thus, N-cyclopropyl-2-chloro-3,4-difluoroaniline (prepared in 10 steps from 3,4-ClFC6H3NH2) was cyclocondensed with (EtO2C)2C:CHOEt to give dihydroquinolonecarboxylate II (R1 = F, R2 = Et), which was aminated with

piperazine to give II (R1 = 1-piperazinyl, R2 = Et). This was saponified to give I (R = H) (III). III had min. inhibitory concns. of 0.025 and 0.05 μg/mL, resp., against the antibiotic-resistant gram-neg. bacteria Serratia marcescens and Pseudomonas aeruginosa, vs. 0.39 and 0.20 μg/mL for ciprofloxacin. III also showed high activity against a variety of gram-pos. bacteria.

RX(19) OF 193 ...AA ===> AB...



AA

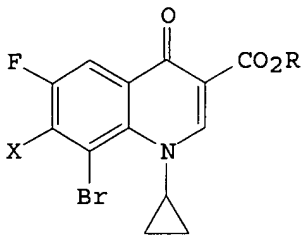
AB

RX(19) RCT AA 101987-88-6
PRO AB 99696-21-6

L7 ANSWER 77 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 105:133766 CASREACT
TITLE: Quinolonecarboxylic acid derivatives
INVENTOR(S): Irikura, Tsutomu; Suzue, Seigo; Hirai, Keiji; Ishizaki, Takayoshi
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 184035	A1	19860611	EP 1985-114373	19851112
EP 184035	B1	19900725		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
JP 61118370	A	19860605	JP 1985-243553	19851030
AU 8549462	A	19860522	AU 1985-49462	19851107
AU 576272	B2	19880818		
HU 40083	A2	19861128	HU 1985-4333	19851113
HU 194833	B	19880328		
IN 164295	A1	19890211	IN 1986-MA922	19861128
PRIORITY APPLN. INFO.:			JP 1984-239124	19841113
			JP 1985-243553	19851030
			IN 1985-MA886	19851105

GI



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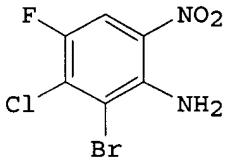
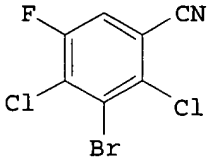
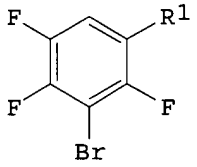


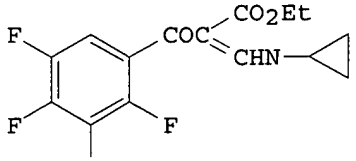
II



III



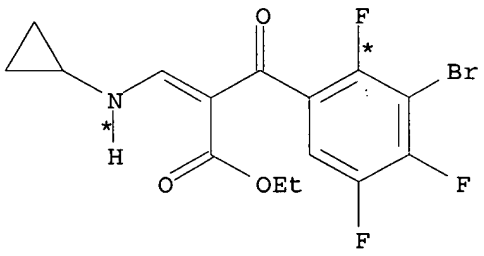
IV



V

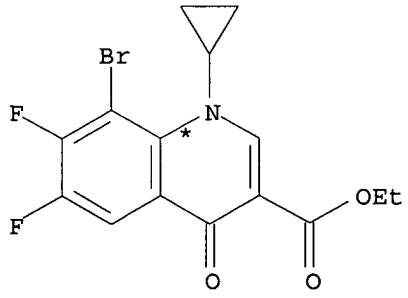
AB Cyclopropylquinolinecarboxylates I (R = H, alkyl; X = halo) are prepared as intermediates for antibacterial agents (no data). Thus, 3,4-ClFC6H3NH2 was acetylated, nitrated, hydrolyzed, and brominated to give halonitroaniline II. This was chlorinated via the diazonium salt, reduced by Fe-HCl, and cyanated via the diazonium tetrafluoroborate to give halobenzonitrile III. Fluorination of III with KF in Me2SO gave bromotrifluorobenzonitrile IV (R1 = cyano), which was hydrolyzed via the amide to give IV (R1 = CO2H). Conversion of the acid to the acid chloride, and condensation of the latter with CH2(CO2Et)2, gave IV [R1 = COCH(CO2Et)2], which was hydrolyzed and decarboxylated to give IV (R1 = COCH2CO2Et). Treatment of the latter with (EtO)3CH-Ac2O gave IV [R1 = COC(:CHOEt)CO2Et], which was condensed with cyclopropylamine to give (cyclopropylamino)(halobenzoyl)acrylate V. Cyclization of V using KF in DMF gave I (R = Et, X = F), which was saponified by H2SO4 in aqueous HOAc to give
I (R = H, X = F).

RX(17) OF 171 ...W ===> X...



W

(17)



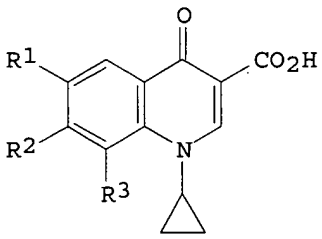
X

RX(17) RCT W 104222-48-2
PRO X 104222-49-3

L7 ANSWER 78 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 105:97345 CASREACT
TITLE: 1-Cyclopropyl-1,4-dihydro-4-oxo-3-quinolinecarboxylic acids
INVENTOR(S): Grohe, Klaus; Schriewer, Michael; Zeiler, Hans Joachim; Metzger, Karl Georg
PATENT ASSIGNEE(S): Bayer A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 41 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3441788	A1	19860515	DE 1984-3441788	19841115
AU 8549177	A	19860522	AU 1985-49177	19851029
AU 572702	B2	19880512		
EP 181588	A2	19860521	EP 1985-114019	19851105
EP 181588	A3	19890201		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4762844	A	19880809	US 1985-795056	19851105
CS 252835	B2	19871015	CS 1985-8132	19851112
FI 8504466	A	19860516	FI 1985-4466	19851113
ES 548843	A1	19861116	ES 1985-548843	19851113
CA 1260478	A1	19890926	CA 1985-495208	19851113
JP 61122272	A	19860610	JP 1985-253881	19851114
ZA 8508733	A	19860730	ZA 1985-8733	19851114
BR 8505734	A	19860812	BR 1985-5734	19851114
HU 40422	A2	19861228	HU 1985-4347	19851114
HU 194178	B	19880128		
PL 145639	B1	19881031	PL 1985-256260	19851114

PRIORITY APPLN. INFO.: DE 1984-3441788 19841115
OTHER SOURCE(S): MARPAT 105:97345
GI



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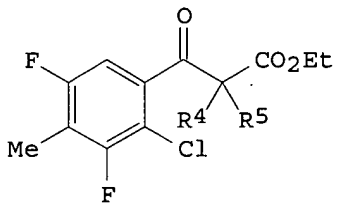
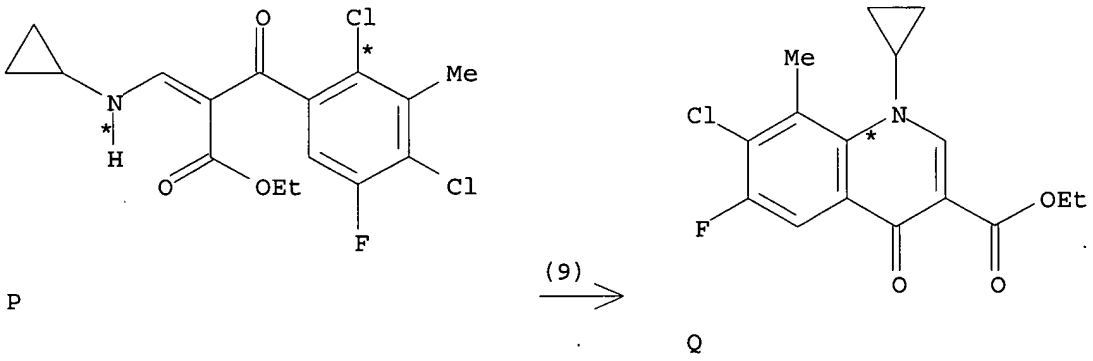


II

AB The title compds. (I; R1-R3 = H, NO2, alkyl, halo) were prepared as medical bactericides. Thus, 2,3,5,4-ClF2MeC6H5COCl was condensed with (EtO2C)2CH2 to give benzoylmalonate II (R4 = H, R5 = CO2Et), which was sequentially hydrolyzed, decarboxylated, ethoxymethylenated with (EtO)3CH, and condensed with cyclopropylamine to give II [R4R5 = (cyclopropylamino)methylene]. The latter compound was cyclized and

deesterified to give I (R1 = R3 = F, R2 = Me) (III). III had a min. inhibitory concentration of 0.06% against Staphylococcus aureus 133.

RX(9) OF 83 P ===> Q...



P

Q

RX(9) RCT P 103877-33-4
PRO Q 103877-47-0

L7 ANSWER 79 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 104:186447 CASREACT
TITLE: 7-(3-Aryl-1-piperazinyl)- and 7-(3-cyclohexyl-1-piperazinyl)quinolone-3-carboxylic acids
INVENTOR(S): Petersen, Uwe; Grohe, Klaus; Zeiler, Hans Joachim; Metzger, Karl
PATENT ASSIGNEE(S): Bayer A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 44 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

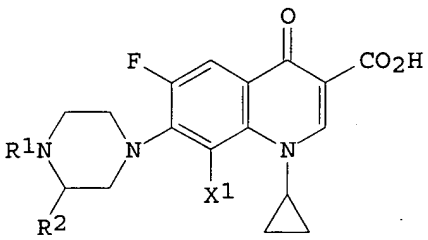
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3420798	A1	19851205	DE 1984-3420798	19840604
CN 85101832	A	19870131	CN 1985-101832	19850401
CN 1014410	B	19911023		
US 4599334	A	19860708	US 1985-735493	19850517
EP 169993	A2	19860205	EP 1985-106252	19850522
EP 169993	A3	19860326		
EP 169993	B1	19881228		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 39488	T	19890115	AT 1985-106252	19850522
NO 8502063	A	19851205	NO 1985-2063	19850523
NO 165105	B	19900917		
NO 165105	C	19901227		
FI 8502205	A	19851205	FI 1985-2205	19850531
FI 82041	B	19900928		
FI 82041	C	19910110		
AU 8543206	A	19851212	AU 1985-43206	19850531
AU 571333	B2	19880414		

JP 61001683	A	19860107	JP 1985-116836	19850531
CA 1248954	A1	19890117	CA 1985-482912	19850531
IL 75370	A	19890331	IL 1985-75370	19850531
IL 85549	A	19890331	IL 1985-85549	19850531
DK 8502496	A	19851205	DK 1985-2496	19850603
DK 162527	B	19911111		
DK 162527	C	19920330		
ZA 8504168	A	19860129	ZA 1985-4168	19850603
ES 543839	A1	19860601	ES 1985-543839	19850603
HU 39175	A2	19860828	HU 1985-2145	19850603
HU 194866	B	19880328		
DD 240016	A5	19861015	DD 1985-276974	19850603
ES 552573	A1	19871101	ES 1986-552573	19860228
ES 552574	A1	19871101	ES 1986-552574	19860228
JP 06279411	A	19941004	JP 1993-342256	19931215

PRIORITY APPLN. INFO.: DE 1984-3420798 19840604
EP 1985-106252 19850522
IL 1985-75370 19850531

OTHER SOURCE(S): MARPAT 104:186447

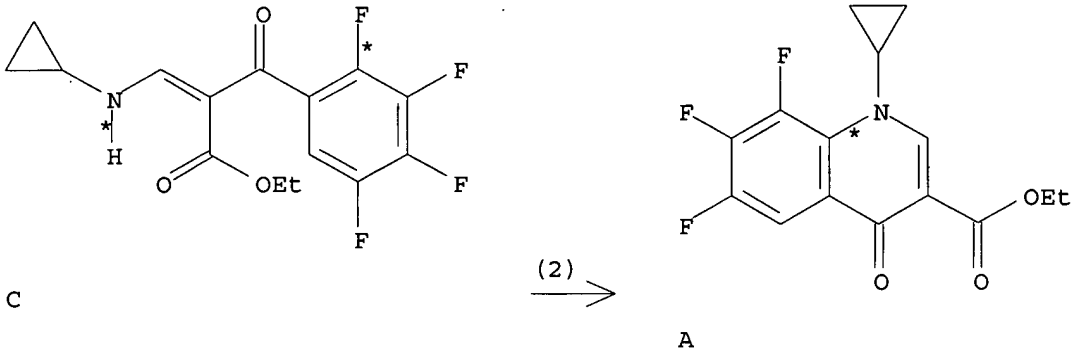
GI



I

AB The title compds. [I; R1 = H, acyl, oxoalkyl, PhCOCH2, (un)substituted alkyl; R2 = (un)substituted cyclohexyl, Ph, methylenedioxycyclohexyl, methylenedioxyphenyl, (tetrahydro)furyl, thienyl; X1 = H, F] were prepared Thus, CH2(CO2Et)2 underwent Grignard benzoylation with 2,4,5-F3C6H2COF to give 2,4,5-F3C6H2COCH(CO2Et)2 which was decarboxylated and condensed with HC(OEt)3 to give 2,4,5-F3C6H2COC(:CHOEt)CO2Et. The latter was aminolyzed with cyclopropylamine, deesterified, and cyclized to give 1-cyclopropyl-6,7-difluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid. This was heated with 2-phenylpiperazine in Me2SO containing DBU to give I (R1 = X1 = H, R2 = Ph) (II). II had a min. inhibitory concentration ≤0.015 mcg/mL against Escherichia coli Neumann.

RX(2) OF 5 C ===> A...



C (2) A

RX(2) RCT C 94695-51-9
PRO A 94242-51-0

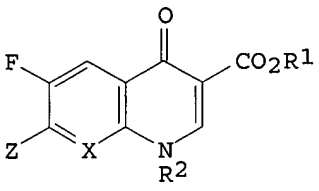
L7 ANSWER 80 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 104:148850 CASREACT
TITLE: Substituted naphthyridine-, quinoline- and benzoxazinecarboxylic acids as antibacterial agents
INVENTOR(S): Hutt, Marland P.; Mich, Thomas F.; Culbertson, Townley P.
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: Eur. Pat. Appl., 64 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 159174	A2	19851023	EP 1985-302479	19850409
EP 159174	A3	19870204		
EP 159174	B1	19911023		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4571396	A	19860218	US 1985-708565	19850311
CA 1340695	C	19990810	CA 1985-477394	19850325
ZA 8502365	A	19851127	ZA 1985-2365	19850328
AU 8540920	A	19851024	AU 1985-40920	19850409
AU 566984	B2	19871105		
AT 68793	T	19911115	AT 1985-302479	19850409
IL 74882	A	19880630	IL 1985-74882	19850411
FI 8501471	A	19851017	FI 1985-1471	19850412
FI 83872	B	19910531		
FI 83872	C	19911230		
DK 8501696	A	19851017	DK 1985-1696	19850415
DK 172796	B1	19990719		
NO 8501501	A	19851017	NO 1985-1501	19850415
NO 162560	B	19891009		
NO 162560	C	19900117		
JP 60260573	A	19851223	JP 1985-78623	19850415
JP 07002739	B	19950118		
HU 37759	A2	19860228	HU 1985-1399	19850415
ES 542239	A1	19860301	ES 1985-542239	19850415

HU 201554	B	19901128	HU 1990-805	19850415
FI 88040	B	19921215	FI 1990-3556	19900713
FI 88040	C	19930325		
PRIORITY APPLN. INFO.:			US 1984-600934	19840416
			US 1985-708565	19850311
			EP 1985-302479	19850409

OTHER SOURCE(S): MARPAT 104:148850

GI



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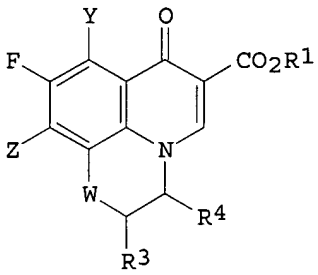
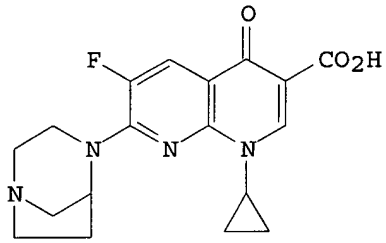


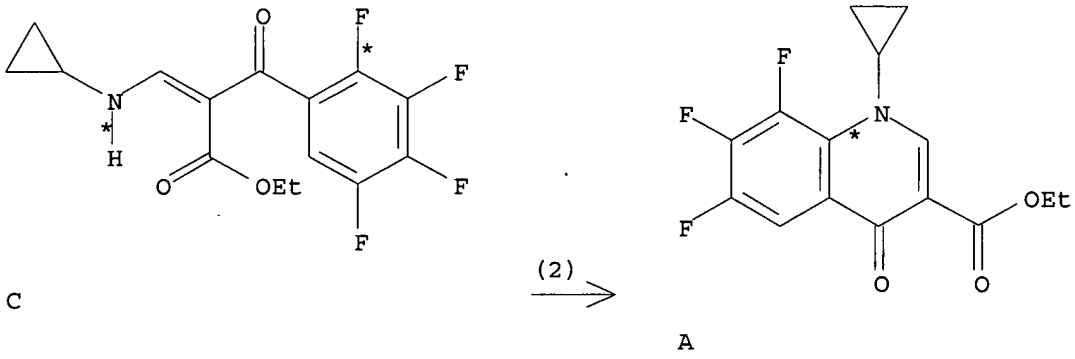
II



III

AB The title compds. [I; R1 = H, alkyl, cation; R2 = CH2:CH, cycloalkyl, (un)substituted alkyl; X = CH, CF, N; Z = bicyclic amino; and II; R1, Z as given; R3, R4 = H, alkyl; W = CH2, O, S, RN; Y = H, F, amino; R = H, (hydroxy)alkyl, PhCH2, 4-H2NC6H4CH2] were prepared Thus, 2.67 g I (R1 = H, R2 = cyclopropyl, X = N, Z = EtSO2), prepared in 11 steps from Et 4-(6-chloro-3-nitro-2-pyridinyl)-1-piperazinecarboxylate, was stirred with 1.58 g 1,4-diazabicyclo[3.2.1]octane-di-HCl at 0°, then 18 h at room temperature, to give 1.04g diazabicyclooctylnaphthyridinecarboxylic acid III. Against Escherichia coli Vogel III had a min. inhibitory concentration of 0.05 μg/mL.

RX(2) OF 21 C ===> A...



C (2) A

RX(2) RCT C 94695-51-9
PRO A 94242-51-0

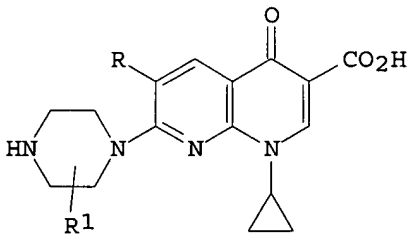
=> d ibib abs fhit 81-88

L7 ANSWER 81 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 104:88622 CASREACT
TITLE: 1,8-Naphthyridine derivatives
INVENTOR(S): Hayakawa, Isao
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60172981	A	19850906	JP 1984-28278	19840217
JP 03074231	B	19911126		
EP 160578	A1	19851106	EP 1985-400270	19850215
EP 160578	B1	19891123		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
JP 63099070	A	19880430	JP 1987-233566	19870917

PRIORITY APPLN. INFO.: JP 1984-28278 19840217
JP 1984-53159 19840319

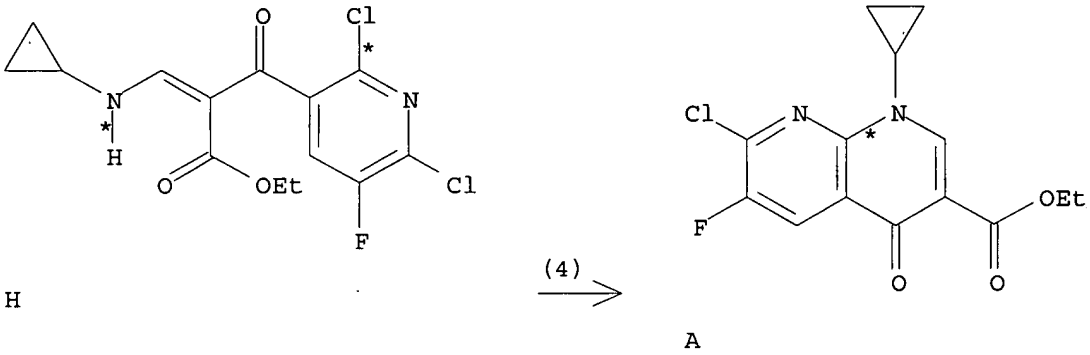
OTHER SOURCE(S): MARPAT 104:88622
GI



I

AB Antibacterial 1,8-naphthyridine derivs. I (R = halo; R1 = lower alkyl, acyl, CONH2, cyano) were prepared Thus, heating 100 mg 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid with 130 mg 2-methylpiperazine in 5 mL pyridine at 60-70° gave 40 mg I (R = F, R1 = 3-Me).

RX(4) OF 36 ...H ===> A...



H

A

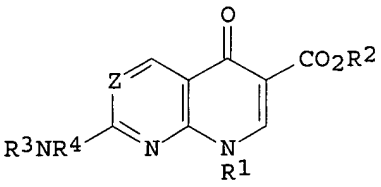
RX(4) RCT H 96568-06-8
RGT I 7646-69-7 NaH
PRO A 96568-07-9

L7 ANSWER 82 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 104:88585 CASREACT
TITLE: Naphthyridine and pyridopyrimidine antibacterial compounds
INVENTOR(S): Chu, Daniel Tim Wo
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: Eur. Pat. Appl., 44 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

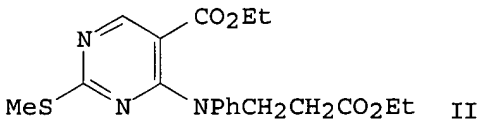
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 153580	A1	19850904	EP 1985-100569	19850121
EP 153580	B1	19890125		
EP 153580	B2	19930317		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
IL 74064	A	19880930	IL 1985-74064	19850115
ZA 8500403	A	19850925	ZA 1985-403	19850117
AT 40366	T	19890215	AT 1985-100569	19850121
AU 8537993	A	19850801	AU 1985-37993	19850123
AU 569603	B2	19880211		
DK 8500345	A	19850727	DK 1985-345	19850125
DK 170212	B1	19950619		
JP 60174786	A	19850909	JP 1985-11121	19850125
JP 63020829	B	19880430		

ES 539880	A1	19860216	ES 1985-539880	19850125
US 4616019	A	19861007	US 1985-784286	19851004
CA 1340782	C	19991012	CA 1985-495684	19851119
PRIORITY APPLN. INFO.:			US 1984-574120	19840126
			US 1984-574226	19840126
			EP 1985-100569	19850121

OTHER SOURCE(S): MARPAT 104:88585
GI



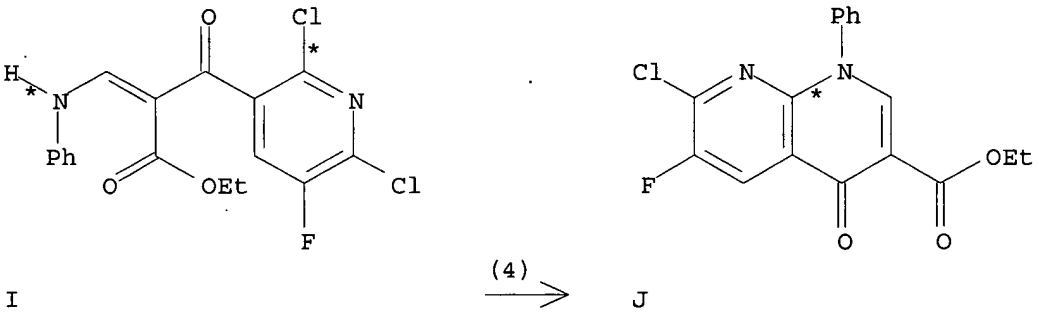
I



II

AB Title compds. I [Z = N, CF; R1 = heteroaryl, (un)substituted Ph; R2 = H, protective group; R3 = H, alkyl; R4 = alkyl; NR3R4 = heterocyclyl], useful as bactericides, were prepared Pyrimidinecarboxylate II underwent cyclization, the product was dehydrogenated and saponified, and subsequent reaction with piperazine gave I (Z = N, R1 = Ph, R2 = H, NR3R4 = piperazino).

RX(4) OF 28 ...I ===> J...



I J

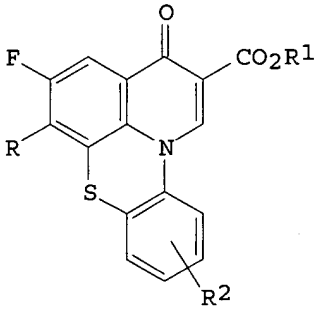
RX(4) RCT I 100426-73-1
PRO J 100426-74-2

L7 ANSWER 83 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 104:19598 CASREACT
TITLE: Quinobenzothiazine antibacterial compounds
INVENTOR(S): Chu, Daniel T.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

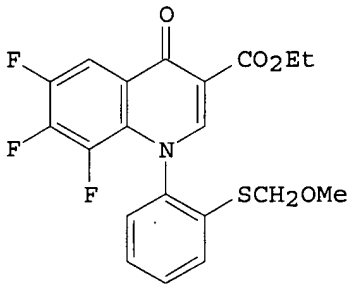
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4533663	A	19850806	US 1984-604338	19840426
JP 60233093	A	19851119	JP 1985-90782	19850426
EP 162333	A1	19851127	EP 1985-105110	19850426
EP 162333	B1	19900627		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
CA 1267649	A1	19900410	CA 1985-480214	19850426
PRIORITY APPLN. INFO.:			US 1984-604190	19840426
			US 1984-604338	19840426
			US 1984-604399	19840426

GI



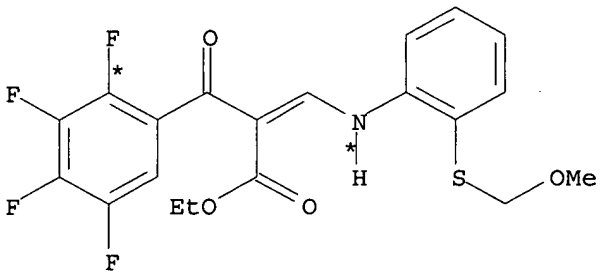
I



II

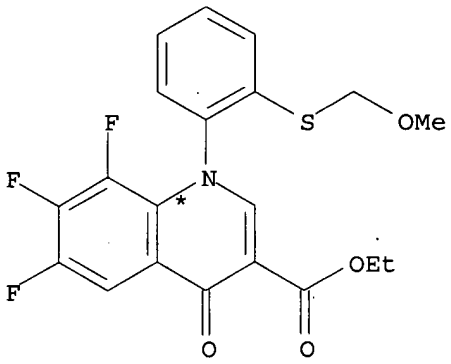
AB Bactericidal (no data) 3H-pyrido[3,2,1-kl]phenothiazine-2-carboxylates I [R = (un)substituted, saturated heterocyclyl; R1 = H, protective group; R2 = H, alkyl, haloalkyl, hydroxyalkyl, CO2H, cyano, halo, amino, NO2, OCH2O, R3Z; R3 = H, alkyl; Z = O, S] were prepared Thus, 2,3,4,5-F4C6HCO2H was converted into its acid chloride and condensed with HO2CCH2CO2Et to give 2,3,4,5-F4C6HCOCH2CO2Et. This was treated successively with HC(OEt)3 and 2-H2NC6H4SCH2OMe, and cyclized by heating with NaH to give phenylquinolinecarboxylate II. The thioether group was cleaved with BCl3 and the product cyclized with NaH to give I (R = F, R1 = Et, R2 = H) which was saponified and condensed with piperazine to give I (R = 1-piperazinyl, R1 = R2 = H).

RX(4) OF 28 ...F ===> G...



F

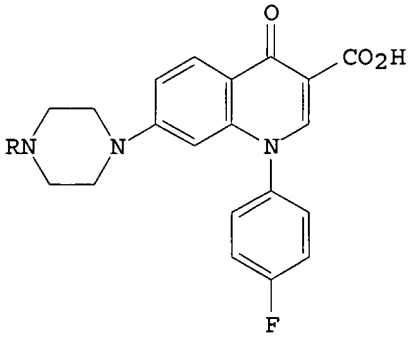
(4) →



G

RX(4) RCT F 99519-76-3
PRO G 99519-77-4

L7 ANSWER 84 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 103:215134 CASREACT
TITLE: Synthesis and structure-activity relationships of novel arylfluoroquinolone antibacterial agents
AUTHOR(S): Chu, Daniel T. W.; Fernandes, Prabhavathi B.; Claiborne, Akiyo K.; Pihuleac, Eva; Nordeen, Carl W.; Maleczka, Robert E., Jr.; Pernet, Andre G.
CORPORATE SOURCE: Antiinfective Res. Div., Abbott Lab., North Chicago, IL, 60064, USA
SOURCE: Journal of Medicinal Chemistry (1985), 28(11), 1558-64
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

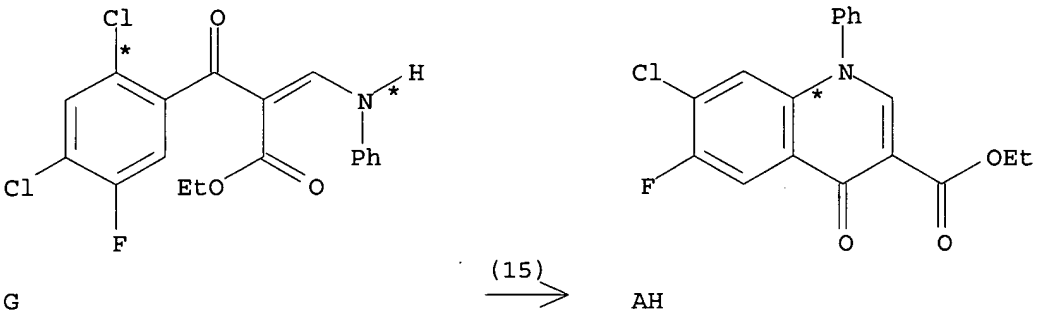


I

AB A series of novel arylfluoroquinolones were prepared with a F atom at the 6-position, substituted amino groups at the 7-position, and substituted Ph groups at the 1-position. Structure-activity relationship (SAR) studies indicated that the in vitro antibacterial potency was greatest when the 1-substituent was p-F or p-HOC6H4, and the 7-substituent was

1-piperazinyl, 4-methyl-1-piperazinyl, or 3-amino-1-pyrrolidinyl. The electronic and spatial properties of the 1-substituent, as well as the steric bulk, played important roles in the antimicrobial potency. The analogs I(R = H, Me) excellent in vitro potency and in vivo efficacy.

RX(15) OF 277 ...G ===> AH...



G AH

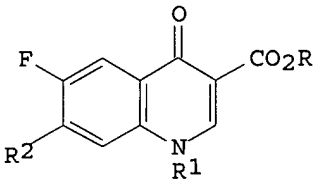
RX(15) RCT G 98126-21-7
RGT D 7646-69-7 NaH
PRO AH 98105-75-0
SOL 110-71-4 (CH2OMe)2

L7 ANSWER 85 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 103:123373 CASREACT
TITLE: Quinoline antibacterial compounds
INVENTOR(S): Chu, Daniel Tim Wo
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 131839	A1	19850123	EP 1984-107688	19840703
EP 131839	B1	19890201		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
IL 72100	A	19880930	IL 1984-72100	19840613
ZA 8404599	A	19850227	ZA 1984-4599	19840618
ES 533916	A1	19851201	ES 1984-533916	19840702
AT 40551	T	19890215	AT 1984-107688	19840703
DK 8403339	A	19850119	DK 1984-3339	19840706
DK 168289	B1	19940307		
AU 8430563	A	19850124	AU 1984-30563	19840713
AU 576323	B2	19880825		
JP 60056959	A	19850402	JP 1984-147042	19840717
JP 01046512	B	19891009		
US 4730000	A	19880308	US 1985-784421	19851007
CA 1337600	C	19951121	CA 1985-495685	19851119
PRIORITY APPLN. INFO.:			US 1983-514716	19830718
			US 1984-574227	19840126
			US 1984-597854	19840409

EP 1984-107688 19840703
US 1985-784421 19851004

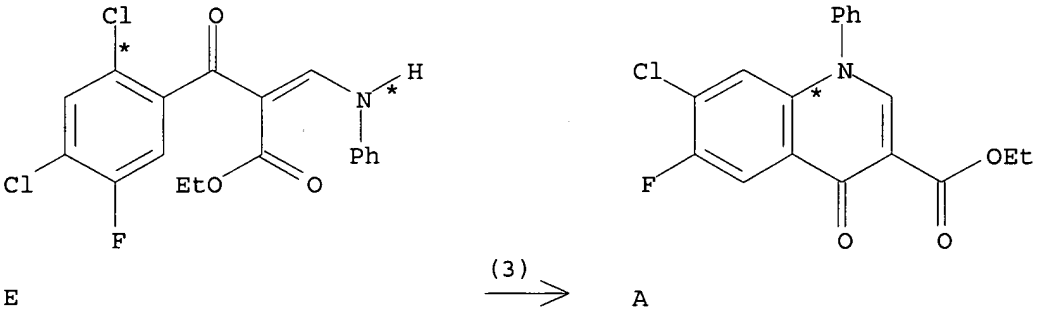
OTHER SOURCE(S): MARPAT 103:123373
GI



I

AB Bactericidal (no data) 6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylates I [R = H, protective group; R1 = heteroaryl, (un)substituted Ph; R2 = amino, aliphatic heterocyclyl] were prepared Thus, 2,4,5-Cl2FC6H2COMe was condensed successively with (EtO)2CO, (EtO)3CH, and PhNH2 to give 2,4,5-Cl2FC6H2COC(CO2Et):CHNHPh. This was refluxed in (CH2OMe)2 with NaH to give I (R = Et, R1 = Ph, R2 = Cl). This was saponified and condensed with piperazine to give I (R = H, R1 = Ph, R2 = 1-piperazinyl).

RX(3) OF 6 E ===> A...



E A

RX(3) RCT E 98126-21-7
PRO A 98105-75-0
CAT 7646-69-7 NaH, 67-56-1 MeOH

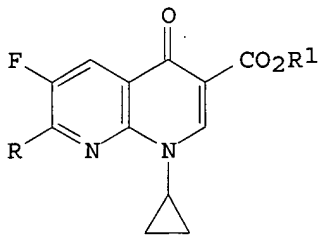
L7 ANSWER 86 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 102:220858 CASREACT
TITLE: 1,8-Naphthyridine derivatives
INVENTOR(S): Matsumoto, Junichi; Nakamura, Shinichi; Miyamoto, Teruyuki; Uno, Hitoshi
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd. , Japan
SOURCE: Eur. Pat. Appl., 69 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

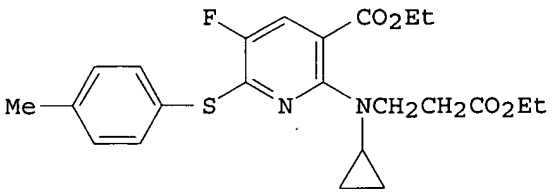
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 132845	A2	19850213	EP 1984-108822	19840725
EP 132845	A3	19850911		
EP 132845	B1	19880413		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 60028978	A	19850214	JP 1983-138000	19830727
JP 03073548	B	19911122		
JP 60260577	A	19851223	JP 1984-117266	19840606
JP 05068477	B	19930929		
CS 274601	B2	19910915	CS 1984-5575	19840719
AU 8430910	A	19850131	AU 1984-30910	19840720
AU 565898	B2	19871001		
US 4649144	A	19870310	US 1984-632853	19840720
ZA 8405708	A	19850327	ZA 1984-5708	19840724
CA 1327580	C	19940308	CA 1984-459527	19840724
AT 33494	T	19880415	AT 1984-108822	19840725
DK 8403651	A	19850128	DK 1984-3651	19840726
DK 160276	B	19910218		
DK 160276	C	19910722		
FI 8402987	A	19850128	FI 1984-2987	19840726
FI 77862	B	19890131		
FI 77862	C	19890510		
HU 34976	A2	19850528	HU 1984-2875	19840726
HU 194561	B	19880229		
DD 228256	A5	19851009	DD 1984-265685	19840726
ES 534624	A1	19851216	ES 1984-534624	19840726
SU 1482527	A3	19890523	SU 1984-3773894	19840726
SU 1442075	A3	19881130	SU 1985-3884501	19850429
SU 1445558	A3	19881215	SU 1985-3885803	19850429
ES 545250	A1	19860516	ES 1985-545250	19850716
PRIORITY APPLN. INFO.:			JP 1983-138000	19830727
			JP 1984-117266	19840606
			EP 1984-108822	19840725

OTHER SOURCE(S): MARPAT 102:220858

GI



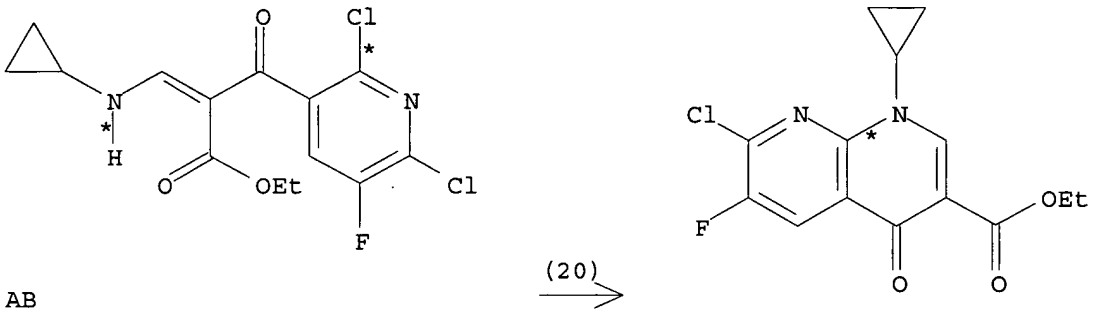
I



II

AB Naphthyridinecarboxylates I [R = (un)substituted 3-aminopyrrolidino; R1 = H, ester group] were prepared Thus, I (R = 4-MeC6H4SO2, R1 = Et), prepared in 7 steps from 2,6-dichloro-5-fluoronicotinonitrile via nicotinate II, was aminated with 3-(acetylamino)pyrrolidine to give I [R = 3-(acetylamino)pyrrolidino, R1 = Et], which was treated with 10% NaOH at 90-110° for 2 h to give I (R = 3-aminopyrrolidino, R1 = H) (II). II inhibited Streptococcus pneumoniae 1 infections in mice with ED50s of 15.2 mg/kg orally and 8.61 mg/kg, i.v.

RX(20) OF 178 ...AB ===> AC



AB

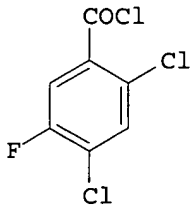
AC

RX(20) RCT AB 96568-06-8
PRO AC 96568-07-9

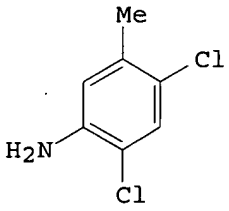
L7 ANSWER 87 OF 103 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 99:53378 CASREACT
TITLE: 2,4-Dichloro-5-fluorobenzoyl chloride
INVENTOR(S): Klauke, Erich; Grohe, Klaus
PATENT ASSIGNEE(S): Bayer A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3142856	A1	19830511	DE 1981-3142856	19811029
DE 3142856	C2	19900111		
US 4439620	A	19840327	US 1982-397958	19820714
JP 58074638	A	19830506	JP 1982-126842	19820722
JP 04050296	B	19920813		

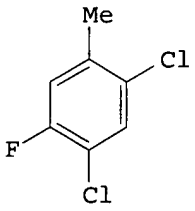
PRIORITY APPLN. INFO.: DE 1981-3142856 19811029
OTHER SOURCE(S): MARPAT 99:53378
GI



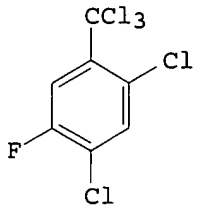
I



II



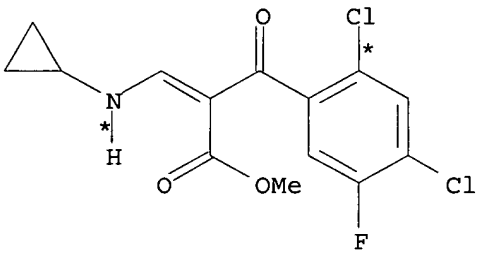
III



IV

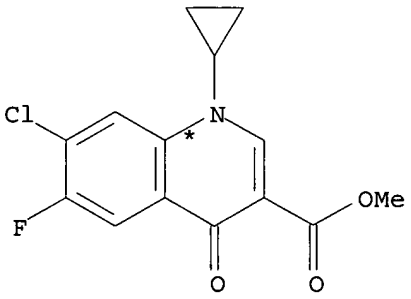
AB The title compound (I) was prepared from II in several ways. Thus, II was diazotized, treated with Me2NH, then HF to give III which was chlorinated to IV, then hydrolyzed to I.

RX(10) OF 41 ...M ===> A...



M

(10)

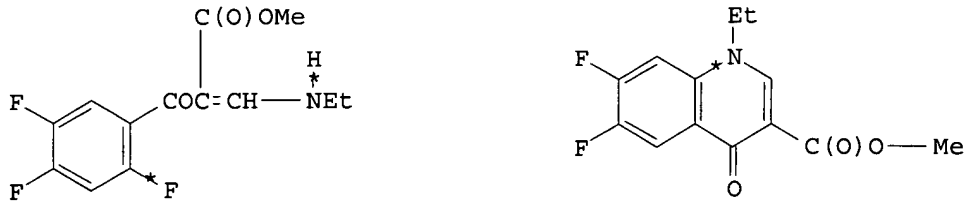


A

RX(10) RCT M 105392-26-5
PRO A 104599-90-8

L7 ANSWER 88 OF 103 CHEMINFORMRX COPYRIGHT 2006 FIZ CHEMIE on STN
AN 200630157 CHEMINFORMRX

RX(10) OF 60 ...P ===> W...



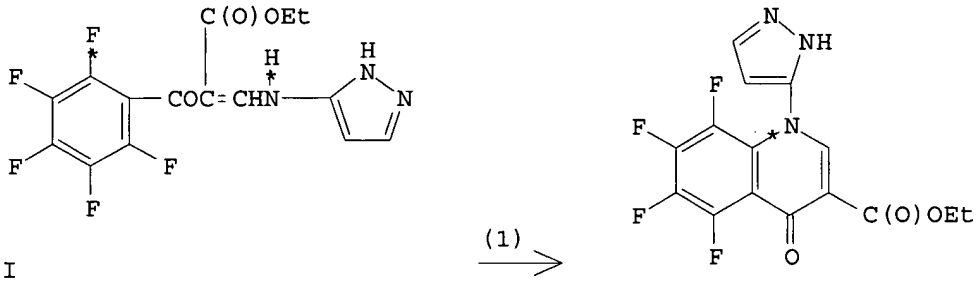
VI (10) VII
YIELD 75.0%

RX(10) RCT VI, 1166713
RGT 1163 (7646-69-7), NaH
SOL 206 (109-99-9), THF
PRO VII, 1166716
YDS 75.0 %
T 25.0 Cel
KW arylation
NTE reaction:VI -> VII, example: 1
CMT #E0100:(Z:E=88:12)

=

L7 ANSWER 89 OF 103 CHEMINFORMRX COPYRIGHT 2006 FIZ CHEMIE on STN
AN 200151042 CHEMINFORMRX
AB Depending on the degree of fluoro-substitution of the benzoyl moiety (pentafluoro or tetrafluoro) and the type of azole substituent (pyrazole or triazole) at the starting acrylates, different cyclization products are obtained by treatment with KF in refluxing MeCN. The triazolo analogue of pentafluoro acrylate (I) fails to give cyclization products of type (II) or (IV). In addition, with a view to potential biologically active compounds, fused pyrimidines (IV) are regioselectively substituted with amines to give compounds (VI).

RX(1) OF 7 A ===> B



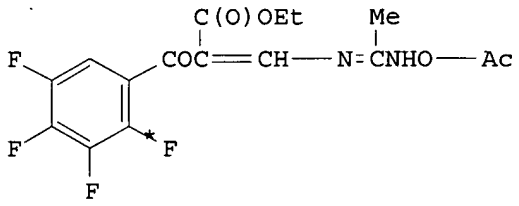
I (1) II
YIELD 70.0%

RX(1) RCT I, 847609
RGT 1138 (7789-23-3), KF
SOL 6 (75-05-8), MeCN
PRO II, 847610
YDS 70.0 %
T.KW REFLUX
TIM 2.0 hr

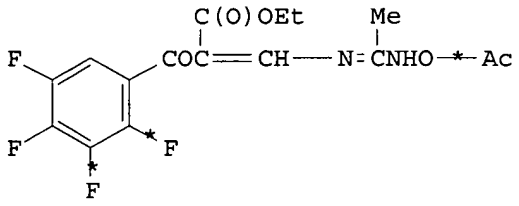
KW arylation
NTE reaction:I -> II

L7 ANSWER 90 OF 103 CHEMINFORMRX COPYRIGHT 2006 FIZ CHEMIE on STN
AN 200035146 CHEMINFORMRX
AB New tricyclic quinolones (IX) are synthesized based on the simultaneous formation of both the pyridone and oxadiazine ring by a double intramolecular displacement reaction of appropriate ketoester (IV). None of the synthesized compounds shows interesting antibacterial activity in vivo against the tested strains with the exception of Klebsiella pneumoniae.

RX(2) OF 18 ...2 D ===> G + H...

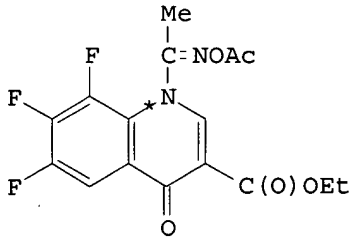


IV

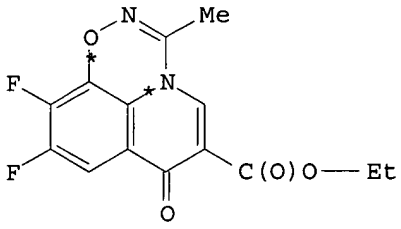


IV

(2) →



V
YIELD 14.0%

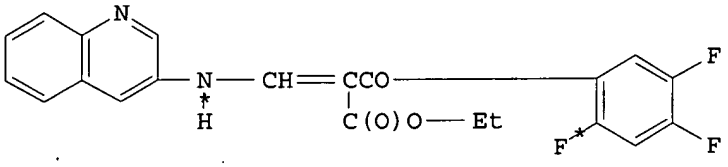


VI
YIELD 22.0%

RX(2) RCT IV, 758929
RGT 768 (584-08-7), K2CO3
SOL 76 (68-12-2), DMF
PRO V, 758930
VI, 758931
YDS 36.0 %
T 50.0 - 60.0 Cel
KW arylation; O-arylation
NTE reaction:IV -> V + VI

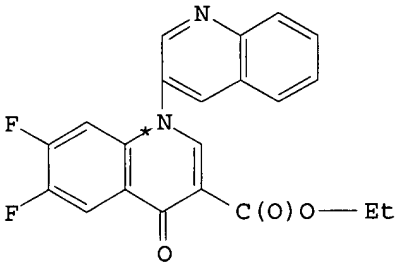
L7 ANSWER 91 OF 103 CHEMINFORMRX COPYRIGHT 2006 FIZ CHEMIE on STN
AN 199846163 CHEMINFORMRX
AB A series of new title compounds (30 examples) are synthesized and evaluated for their anti-HIV-RT activities. Several compounds in this series exhibit better activity than the reference drug atevirdine.

RX(4) OF 42 ...D ===> L...



IV

(4)

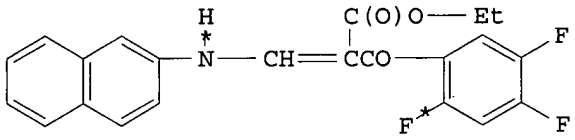


V
YIELD 95.0%

RX(4) RCT IV, 636080
RGT 768 (584-08-7), K2CO3
541 (17455-13-9), 18-crown-6
SOL 6 (75-05-8), MeCN
PRO V, 636083
YDS 95.0 %
T.KW REFLUX
KW arylation
NTE reaction:IV -> V, example: 1

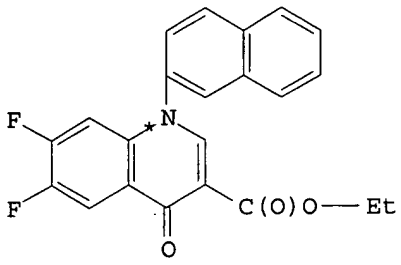
L7 ANSWER 92 OF 103 CHEMINFORMRX COPYRIGHT 2006 FIZ CHEMIE on STN
AN 199830164 CHEMINFORMRX

RX(3) OF 20 ...D ===> I...



IV

(3)

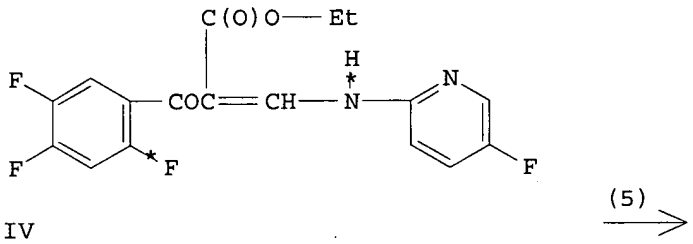


V
YIELD 98.0%

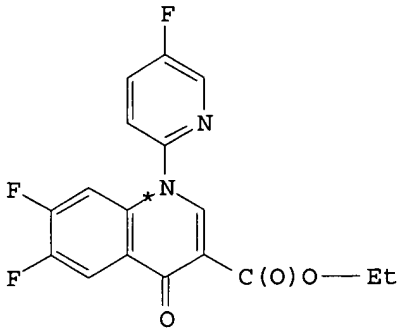
RX(3) RCT IV, 609555
RGT 768 (584-08-7), K2CO3
541 (17455-13-9), 18-crown-6
SOL 6 (75-05-8), MeCN
PRO V, 609557
YDS 98.0 %
T.KW REFLUX
KW arylation
NTE reaction:IV -> V, example: 1

L7 ANSWER 93 OF 103 CHEMINFORMRX COPYRIGHT 2006 FIZ CHEMIE on STN
AN 199745165 CHEMINFORMRX
AB A variety of new quinolones bearing fluorinated pyridyl groups at N1 (cf. (VIII), (IX); 18 examples) are synthesized and evaluated for their antibacterial activity. Derivative (VIIIa) displays a moderate in vitro antibacterial activity, but it shows very excellent pharmacokinetic profiles, so that (VIIIa) shows dramatic increased in vivo efficacy.

RX(5) OF 32 ...D ===> L...



IV

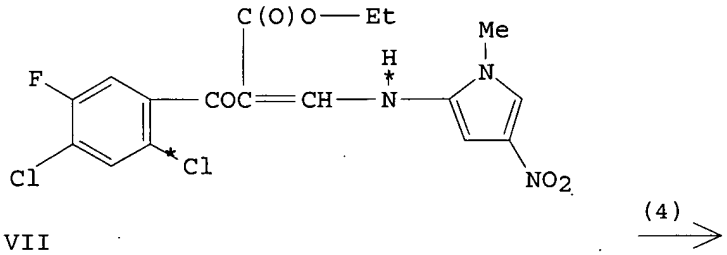


V
YIELD 98.0%

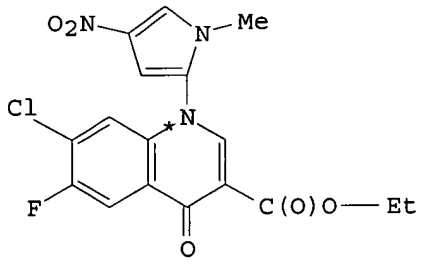
RX(5) RCT IV, 562115
RGT 768 (584-08-7), K2CO3
SOL 76 (68-12-2), DMF
PRO V, 562120
YDS 98.0 %
T 80.0 - 90.0 Cel
KW arylation
NTE reaction:IV -> V, example: 1

L7 ANSWER 94 OF 103 CHEMINFORMRX COPYRIGHT 2006 FIZ CHEMIE on STN
AN 199320217 CHEMINFORMRX
AB Starting with 2,4-dichlorofluorobenzene (I), several heterosubstituted quinolines such as (X) are synthesized by an intramolecular nucleophilic displacement and cyclization reaction. The compounds are tested for their antibacterial activities against Escherichia coli and Staphylococcus aureus, and the derivative (Xb) shows significant activity against the latter microorganism.

RX(4) OF 34 ...H ===> L...



VII

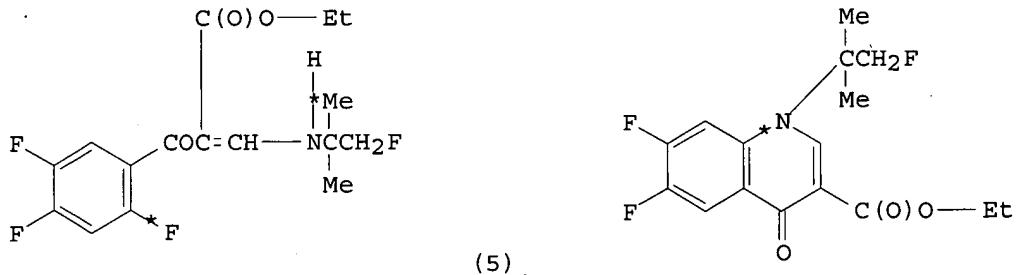


VIII
YIELD 96.0%

RX(4) RCT VII, 228488 (142509-39-5)
RGT 768 (584-08-7), K2CO3
SOL 76 (68-12-2), DMF
PRO VIII, 228490 (142509-40-8)
YDS 96.0 %
T 130.0 Cel
TIM 1.0 hr
KW arylation
NTE reaction:VII -> VIII, example: 1

L7 ANSWER 95 OF 103 CHEMINFORMRX COPYRIGHT 2006 FIZ CHEMIE on STN
AN 199122157 CHEMINFORMRX
AB Reaction of the enol ethers (I) with the amine hydrochlorides (II) forms the corresponding enamines (III) which are cyclized and coupled with secondary amines such as (V) to produce a series of twenty-four fluoronaphthyridines and -quinolones such as (VII) after hydrolysis. Derivatives with the monofluoro-tert-butyl substituents such as (VIIa) show good antibacterial activity in vitro, but not in vivo.

RX(5) OF 40 ...C ===> L...



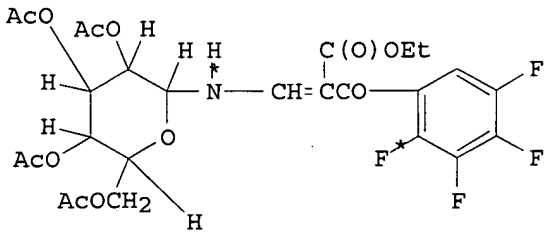
III

IV
YIELD 33.0%

RX(5) RCT III, 156459
RGT 1163 (7646-69-7), NaH
SOL 80 (123-91-1), dioxane
PRO IV, 156466 (130435-38-0)
YDS 33.0 %
T.KW REFLUX
TIM 4.0 hr
KW arylation
NTE reaction:III -> IV, example: 1

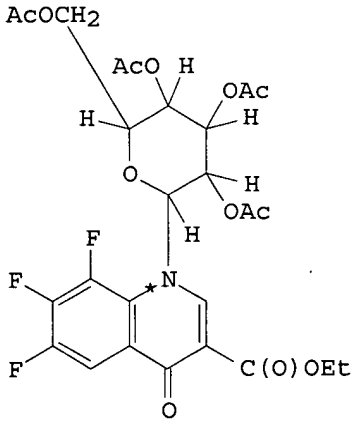
L7 ANSWER 96 OF 103 CHEMINFORMRX COPYRIGHT 2006 FIZ CHEMIE on STN
AN 199119274 CHEMINFORMRX
AB The ethoxyvinyl tetrafluorophenyl ketone (I) is coupled with 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosylamine (II) in hot ethanol to give the enamine (III) which undergoes intramolecular cyclization in the presence of a base, producing the quinolone (IV).

RX(2) OF 3 ...C ===> E



III

(2) ⟶



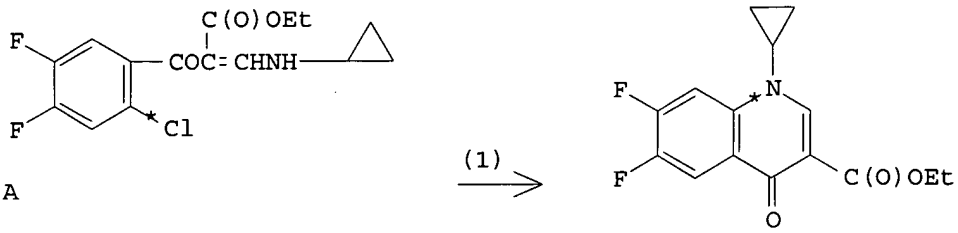
IV
YIELD 68.0%

RX(2) RCT III, 354710 (133491-09-5;133491-10-8), CHIRAL
RGT 1163 (7646-69-7), NaH
SOL 206 (109-99-9), THF
PRO IV, 354711 (133491-11-9), CHIRAL
YDS 68.0 %
KW arylation
NTE reaction:III* -> IV*
CMT Ratio = 1:10 for products 1,2

L7 ANSWER 97 OF 103 DJSMONLINE COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSIONNUMBER: 1998:0844 DJSMONLINE
TITLE: 4(1H)-QUINOLONES FROM 2-(O-HALOGENOAROYL)ENAMINES . IMPROVED PROCEDURE
PATENT ASSIGNEE: Ihara Chem Ind Co Ltd
PATENT INFORMATION: JP 09309880
DOCUMENT TYPE: Patent

VOLUME/ISSUE: 24-4
OTHER SOURCE: WPI 1998-071867
AN 1998:0844 DJSMONLINE
AB Cf. 1989:77105E; 1986:77864B. Products are obtained in a high state of purity, and the use of a titanium(IV) salt is avoided (cf. 1993:77854J/76599J). For further examples, and esters as medium, see citation 1.

RX(1) OF 1 A ===> B



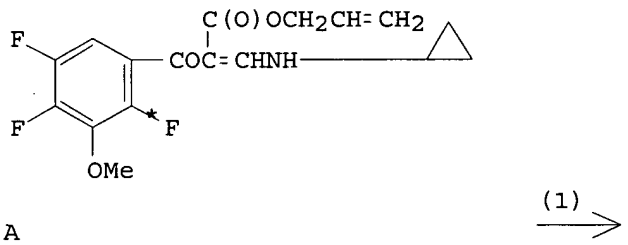
A

B
YIELD 93.0%

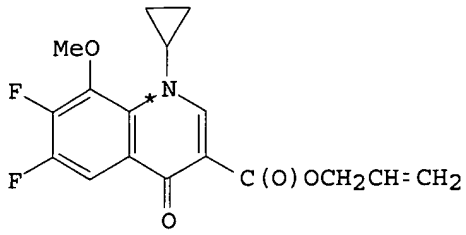
RX(1) RCT A, 97835
SOL 31, EtOAc
CAT 79, NaH; 60% In mineral oil
PRO B, 97836; Purity 99.8%
T 60.0 Cel
TIM 4.5 hr
CMT Path A

L7 ANSWER 98 OF 103 DJSMONLINE COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSIONNUMBER: 1993:77854J DJSMONLINE
TITLE: 4(1H)-QUINOLONES FROM 2-(O-HALOGENOAROYL)ENAMINES
PATENT ASSIGNEE: Ube Ind Ltd
PATENT INFORMATION: JP 05051365
DOCUMENT TYPE: Patent
VOLUME/ISSUE: 19-12
OTHER SOURCE: WPI 1993-112748
AN 1993:77854J DJSMONLINE
AB Cf. 1989:77105E. For further examples, see citation 1.

RX(1) OF 1 A ===> B



A

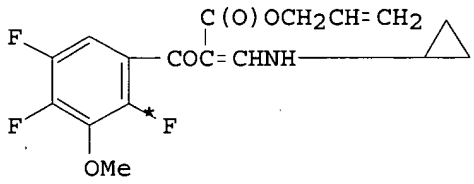


B
YIELD 87.0%

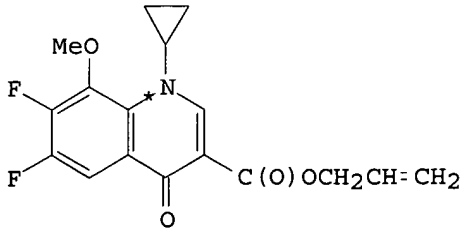
RX(1) RCT A, 9822
SOL 26, Toluene
CAT 5255, Ti-tetraallyloxide
PRO B, 11250
CMT Reflux
CMT Path A

L7 ANSWER 99 OF 103 DJSMONLINE COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSIONNUMBER: 1993:76599J DJSMONLINE
TITLE: 4-PYRIDONE RING FROM 2-(O-HALOGENOAROYL)ENAMINES . 4(1H)-QUINOLONES AND 1,8-NAPHTHYRIDIN-4-ONES
PATENT ASSIGNEE(1): Ube Ind Ltd
PATENT ASSIGNEE(2): Wentland, M. P.
PATENT INFORMATION: JP 05051365
DOCUMENT TYPE: Patent
VOLUME/ISSUE: 19-7
OTHER SOURCE: WPI 1993-112748
AN 1993:76599J DJSMONLINE
AB Cf. 1989:77105E. For further examples, also 1,8-naphthyridin-4-ones, see citation 1. Also, for procedure with added primary amines via transamination, see citation 2.

RX(1) OF 1 A ===> B



A (1) ⟶

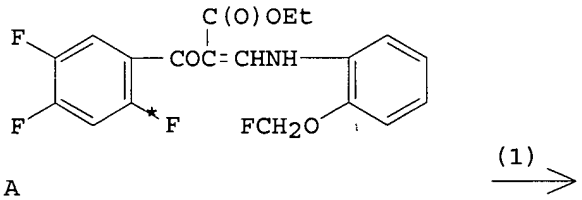


B
YIELD 87.0%

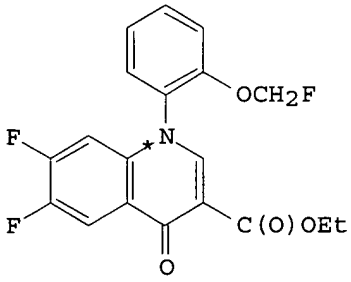
RX(1) RCT A, 9822
SOL 26, Toluene
CAT 5255, Ti-tetraallyloxide
PRO B, 11250
CMT Reflux
CMT Path A

L7 ANSWER 100 OF 103 DJSMONLINE COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSIONNUMBER: 1989:77105E DJSMONLINE
TITLE: 4(1H)-QUINOLONES FROM 2-(O-FLUOROAROYL)ENAMINES
AUTHOR: Xiao, W.
SOURCE: J Pharm Sci, 78(7), p.585-8 (1989)
CODEN: JPMSAE ISSN: 0022-3549
DOCUMENT TYPE: Journal
VOLUME/ISSUE: 15-9
AN 1989:77105E DJSMONLINE
AB Cf. 1987:75694C. For further examples, (70-91%), see citation 1.

RX(1) OF 1 A ===> B



A



B
YIELD 88.0%

RX(1) RCT A, 34399
SOL 23, DMF

CAT 80, Na2CO3
PRO B, 34400
T 22.0 - 100.0 Cel
TIM 1.0 hr
ATM N2
CMT Path A

=> d 101-103 all

L7 ANSWER 101 OF 103 PS COPYRIGHT 2006 THIEME on STN
AN 267209
DED 20030618
CN GENERIC: Sparfloxacin
CN SYNONYM: AT-4140; Ci-978; CP 103826; PD-131501; RP-64206
CN SYSTEMATIC: cis-5-Amino-1-cyclopropyl-7-(3,5-dimethyl-1-piperazinyl)-6,8-difluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid
TN Zagam; Spara; Zagam
CC J01MA09
THER antibiotic
RN 110871-86-8
MF C19H22F2N4O3
MW 392.41
LD50 >5 g/kg (R, p. o.); >2 g/kg (R, s. c.);>2 g/kg (M, p. o.); >2 g/kg (M, s. c.);> 600 mg/kg (dog, p. o.)

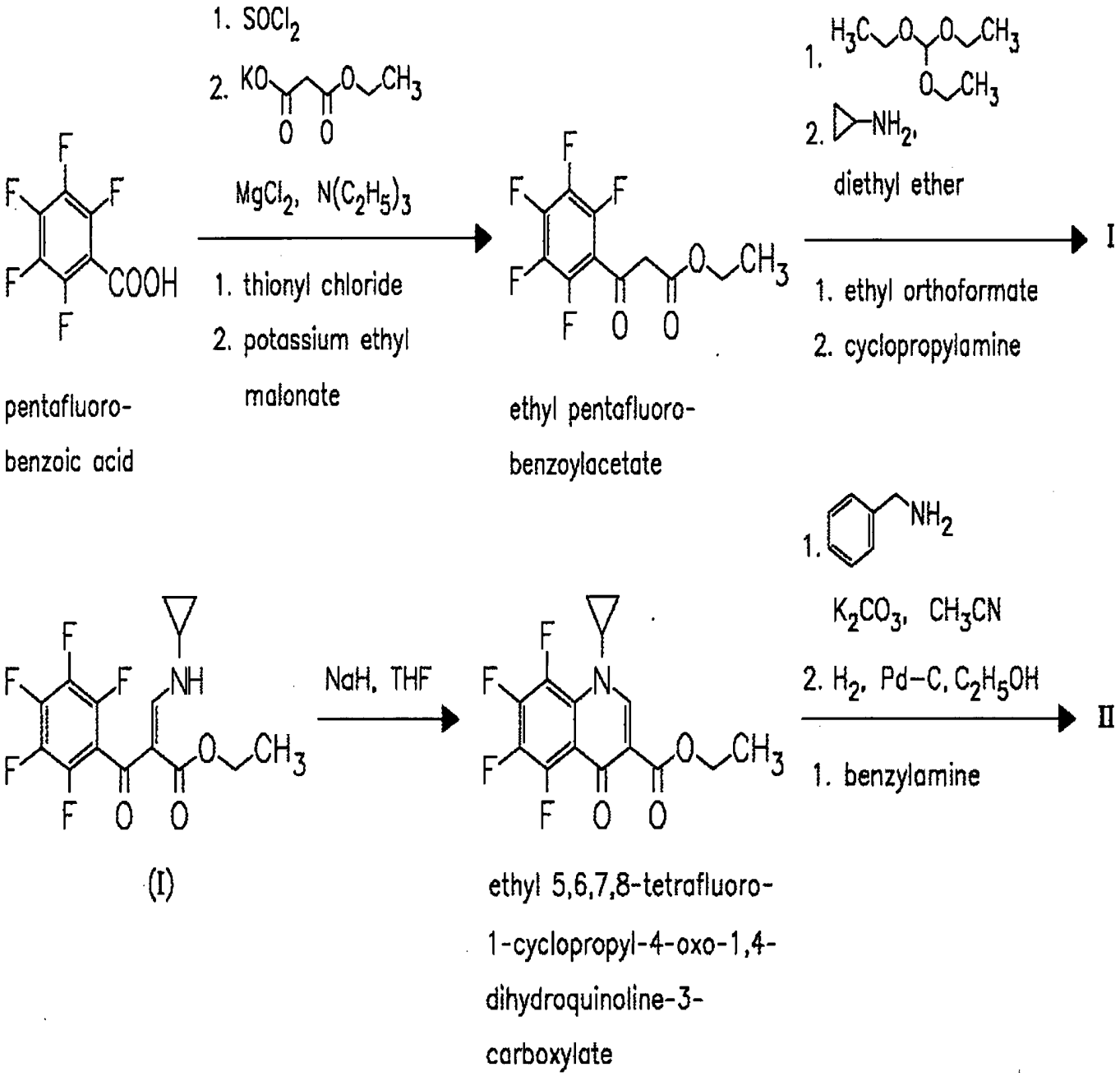
DEF Amino acids (other)
DEF Quinolinecarboxylic acids, 1-Cyclopropyl-1,4-dihydro-4-oxo-3-quinolinecarboxylic acids
DEF Quinolinecarboxylic acids, Fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acids

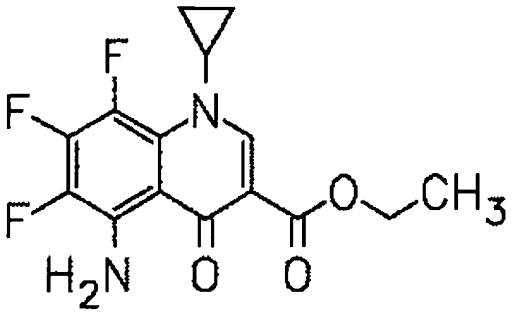
TRD

LNY	LNC	TN	CO	STA	COM
	FR	Zagam	Specia		
	JP	Spara	Dainippon		
	US	Zagam	Rhone-Poulenc Rorer	wfm	

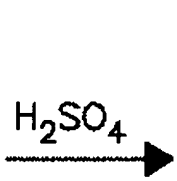
FRM f. c. tabl. 200 mg; tabl. 100 mg, 150 mg

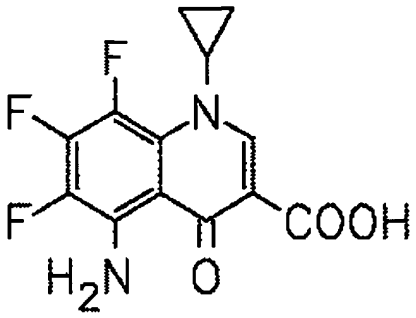
PRE


1. $SOCl_2$
2. KO
O O
CH_3
$MgCl_2$, $N(C_2H_5)_3$
1. thionyl chloride
2. potassium ethyl malonate
1.
H_3C O O CH_3
O CH_3
2. NH_2,
diethyl ether
1. ethyl orthoformate
2. cyclopropylamine
I
F
COOH
pentafluoro-benzoic acid
ethyl pentafluoro-benzoylacetate
1.
NH_2
K_2CO_3, CH_3CN
2. H_2, Pd–C, C_2H_5OH
1. benzylamine
II
NaH, THF
NH
N
(I)
ethyl 5,6,7,8-tetrafluoro-1-cyclopropyl-4-oxo-1,4-dihydroquinoline-3-carboxylate



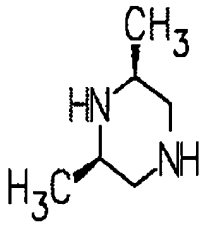
(II)



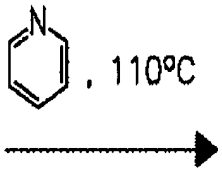


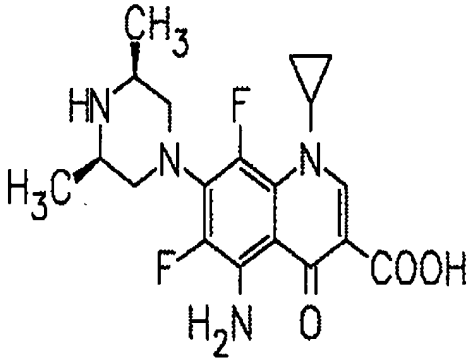
5-amino-1-cyclopropyl-6,7,8-trifluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (III)

III +



cis-2,6-dimethyl-piperazine





Sparfloxacin

INT

RN.INT	MF.INT	CN.INT
103772-14-1	C13H9F3N2O3	5-amino-1-cyclopropyl-6,7,8-trifluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid; 3-Quinolinecarboxylic acid, 5-amino-1-cyclopropyl-6,7,8-trifluoro-1,4-dihydro-4-oxo-
100-46-9	C7H9N	benzylamine; Benzenemethanamine
765-30-0	C3H7N	cyclopropylamine; Cyclopropanamine
21655-48-1	C6H14N2	cis-2,6-dimethylpiperazine; Piperazine, 2,6-dimethyl-, (2R,6S)-rel-
103772-13-0	C15H13F3N2O3	ethyl 5-amino-1-cyclopropyl-6,7,8-trifluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylate; 3-

		Quinolinecarboxylic acid, 5-amino-1-cyclopropyl-6,7,8-trifluoro-1,4-dihydro-4-oxo-, ethyl ester
107564-01-2	C15H12F5NO3	ethyl α-[(cyclopropylamino)methylene]-2,3,4,5,6-pentafluoro-β-oxobenzenepropanoate; Benzenepropanoic acid, α-[(cyclopropylamino)methylene]-2,3,4,5,6-pentafluoro-β-oxo-, ethyl ester
122-51-0	C7H16O3	ethyl orthoformate; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-
3516-87-8	C11H7F5O3	ethyl pentafluorobenzoylacetate; Benzenepropanoic acid, 2,3,4,5,6-pentafluoro-β-oxo-, ethyl ester
107564-02-3	C15H11F4NO3	ethyl 5,6,7,8-tetrafluoro-1-cyclopropyl-4-oxo-1,4-dihydroquinoline-3-carboxylate; 3-Quinolinecarboxylic acid, 1-cyclopropyl-5,6,7,8-tetrafluoro-1,4-dihydro-4-oxo-, ethyl ester
122-51-0	C7H16O3	orthoformic acid triethyl ester; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-
602-94-8	C7HF5O2	pentafluorobenzoic acid; Benzoic acid, pentafluoro-
6148-64-7	C5H7KO4	potassium ethyl malonate; Propanedioic acid, monoethyl ester, potassium salt
6148-64-7	C5H7KO4	potassium monoethyl malonate; Propanedioic acid, monoethyl ester, potassium salt
122-51-0	C7H16O3	triethoxymethane; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-
122-51-0	C7H16O3	triethyl orthoformate; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-

RE

(1) Miyamoto, T. et al.: J. Med. Chem. (JMCMAR) 33, 1645-1656 (1990).
(2) US 4 795 751 (Dainippon; 3.1.1989; J-prior. 29.10.1985, 17.12.1985, 17.2.1986).
synthesis of ethyl pentafluorobenzoylacetate:
(3) EP 221 463 (Dainippon; appl. 23.10.1986; J-prior. 29.10.1985).
(4) Clay, R.J.; Collom, T.A.; Karride, G.L.; Wemple, J.: Synthesis (SYNTBF) 3, 290 (1993)

L7 ANSWER 102 OF 103 PS COPYRIGHT 2006 THIEME on STN

AN 265600
DED 20030618
CN GENERIC: Tosufloxacin
CN SYSTEMATIC: (±)-7-(3-amino-1-pyrrolidinyl)-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid
TN Osex; Tosuxacin
THER antibiotic, quinolone antibacterial, gyrase inhibitor
RN 108138-46-1
MF C19H15F3N4O3
MW 404.35

DEF Amino acids (other)
DEF Fluorocarboxylic acids
DEF 1,8-Naphthyridines, 1,4-Dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acids

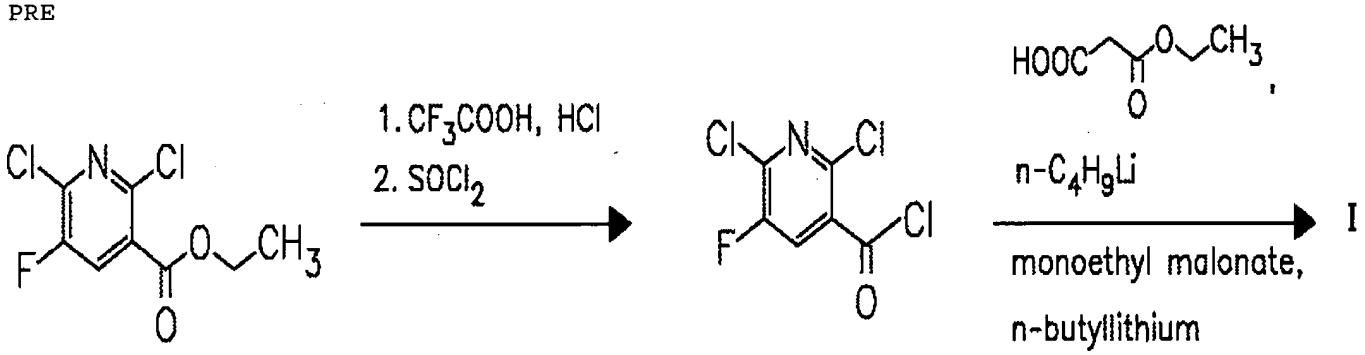
DEF Pyrrolidines, aminopyrrolidines
DEF p-Toluenesulfonates (4-Methylbenzenesulfonates)
DRV CN.DRV monotosylate
RN.DRV 115964-29-9
MF.DRV C19H15F3N4O3 C7H8O3S
MW.DRV 576.55
LD50.DRV 196 mg/kg (M, i.v.); >6 g/kg (M, p.o.);270 mg/kg (R, i.v.); >6 g/kg (R, p.o.);>3 g/kg (dog, p.o.)

TRD

LNY	LNC	TN	CO	STA	COM
	JP	Osex	Toyama Chemical		
	JP	Tosuxacin	Dainippon		

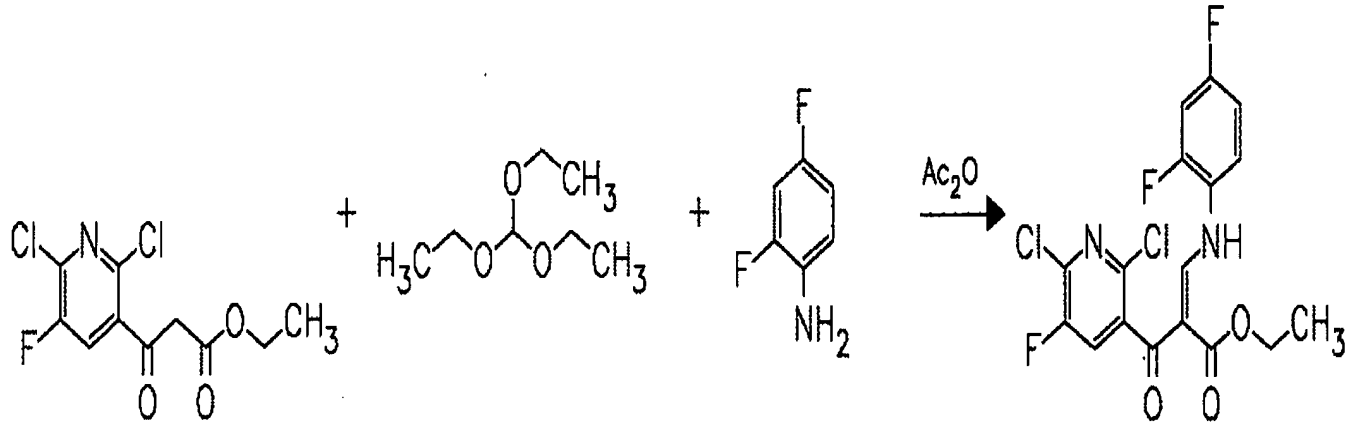
FRM tabl. 75 mg, 150 mg (as tosylate)

PRE



ethyl 2,6-dichloro-5-fluoronicotinate

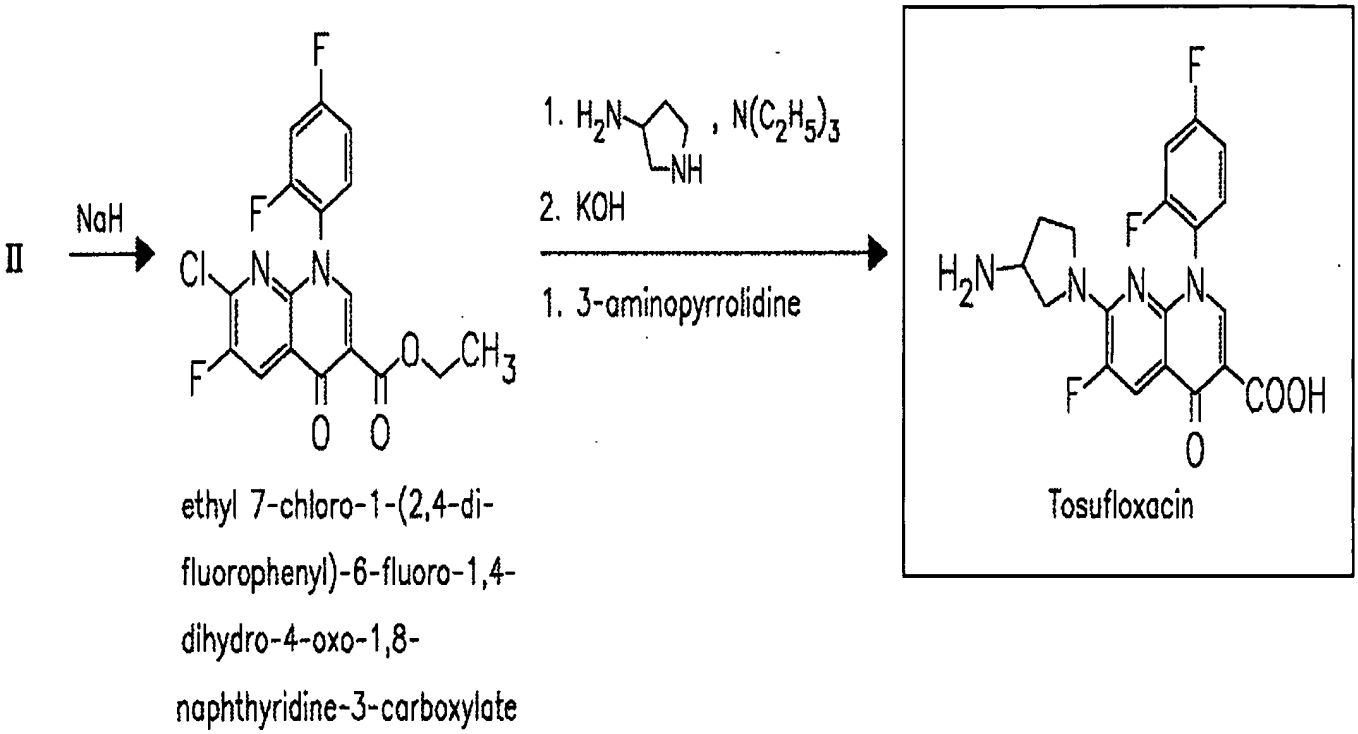
2,6-dichloro-5-fluoronicotinoyl chloride



ethyl 2,6-dichloro-5-fluoronicotinoylacetate (I)

triethyl orthoformate

2,4-difluoroaniline



ethyl 7-chloro-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylate

INT

RN.INT	MF.INT	CN.INT
79286-79-6	C4H10N2	3-aminopyrrolidine; 3-Pyrrolidinamine
100490-99-1	C17H11Cl2F3N2O3	2,6-dichloro-α-[[(2,4-difluorophenyl)amino]methylene]-5-fluoro-β-oxo-3-pyridinepropanoic acid ethyl ester; 3-Pyridinepropanoic acid, 2,6-dichloro-α-[[(2,4-difluorophenyl)amino]methylene]-5-fluoro-β-oxo-, ethyl ester
96568-02-4	C6HCl3FNO	2,6-dichloro-5-fluoronicotinoyl chloride; 3-Pyridinecarbonyl chloride, 2,6-dichloro-5-fluoro-
367-25-9	C6H5F2N	2,4-difluoroaniline; Benzenamine, 2,4-difluoro-
100491-29-0	C17H10ClF3N2O3	ethyl 7-chloro-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylate; 1,8-Naphthyridine-3-carboxylic acid, 7-chloro-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-, ethyl ester
100491-29-0	C17H10ClF3N2O3	ethyl 7-chloro-1-(2,4-difluorophenyl)-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylate; 1,8-Naphthyridine-3-carboxylic acid, 7-chloro-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-, ethyl ester
82671-03-2	C8H6Cl2FNO2	ethyl 2,6-dichloro-5-fluoronicotinate; 3-Pyridinecarboxylic acid, 2,6-dichloro-5-fluoro-, ethyl ester

96568-04-6	C10H8Cl2FNO3	ethyl 2,6-dichloro-5-fluoronicotinoylacetate; 3-Pyridinepropanoic acid, 2,6-dichloro-5-fluoro-β-oxo-, ethyl ester
122-51-0	C7H16O3	ethyl orthoformate; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-
1071-46-1	C5H8O4	monoethyl malonate; Propanedioic acid, monoethyl ester
122-51-0	C7H16O3	orthoformic acid triethyl ester; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-
122-51-0	C7H16O3	triethoxymethane; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-
122-51-0	C7H16O3	triethyl orthoformate; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-

RE

(1) DE 3 514 076 (Toyama; appl. 31.10.1985; J-prior. 26.4.1984).
(2) US 4 704 459 (Toyama; 3.11.1987; appl. 17.1.1986; J-prior. 23.1.1985, 18.2.1985, 7.3.1985, 3.4.1985, 8.5.1985, 14.6.1985).
(3) Chu, D.T.W. et al.: J. Med. Chem. (JMCMAR) 29, 2363 (1986).
synthesis of ethyl 2,6-dichloro-5-fluoronicotinate:
(4) Narita, H. et al.: Yakugaku Zasshi (YKKZAJ) 106, 802 (1986).
alternative synthesis:
(5) JP 82/72 981 (H. Matsumoto et al.; appl. 7.5.1982).
(6) EP 302 372 (Abbott; appl. 8.2.1989; USA-prior. 4.8.1987).
(7) BE 904 086 (Toyama; appl. 14.6.1985; J-prior. 23.1.1985).

L7 ANSWER 103 OF 103 PS COPYRIGHT 2006 THIEME on STN
AN 265008
DED 20030618
CN GENERIC: Ciprofloxacin
CN SYNONYM: Bay-o-9867
CN SYSTEMATIC: 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid
TN Ciloxan; Ciprobay; Ciflox; Uniflox; Ciloxan; Ciproxin; Ciproxin; Flociprin; Oftacilox; Ciproxan; Ciloxan; Cipro
CC J01MA02; S03AA07
THER antibiotic
RN 85721-33-1
MF C17H18FN3O3
MW 331.35
LD50 122 mg/kg (M, i.v.); 5 g/kg (M, p.o.);207 mg/kg (R, i.v.); >2 g/kg (R, p.o.)

DEF Quinolinecarboxylic acids, 1,4-Dihydro-4-oxo-3-quinolinecarboxylic acids
DEF Quinolinecarboxylic acids, Fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acids
DRV CN.DRV monohydrate
RN.DRV 113078-43-6
MF.DRV C17H18FN3O3 H2O
MW.DRV 349.36
DRV CN.DRV monohydrochloride
RN.DRV 93107-08-5
MF.DRV C17H18FN3O3 HCl
MW.DRV 367.81
DRV CN.DRV hydrochloride
RN.DRV 86483-48-9

	MF.DRV	C17H18FN3O3 xHCl
	MW.DRV	unspecified
	LD50.DRV	258 mg/kg (M, i.v.); >5 g/kg (M, p.o.);300 mg/kg (R, i.v.); >5 g/kg (R, p.o.)
DRV	CN.DRV	lactate (1:1)
	RN.DRV	97867-33-9
	MF.DRV	C17H18FN3O3 C3H6O3
	MW.DRV	421.43

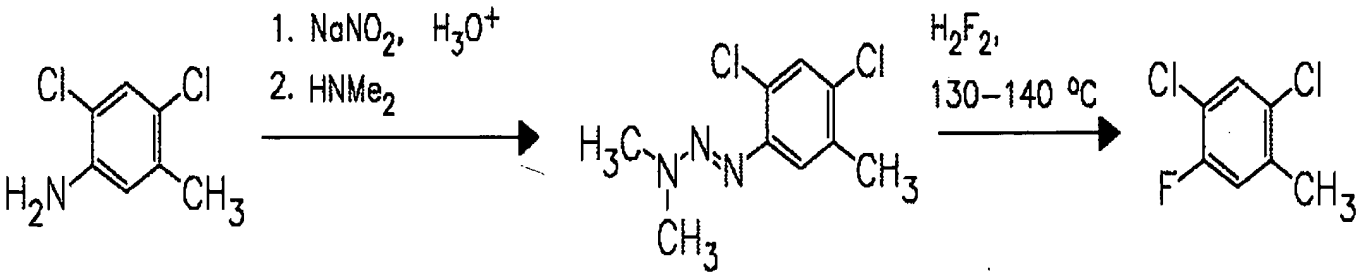
TRD

LNY	LNC	TN	CO	STA	COM
	DE	Ciloxan	Alcon		
1987	DE	Ciprobay	Bayer Vital		
	FR	Ciflox	Bayer		
	FR	Uniflox	Bayer		
	GB	Ciloxan	Alcon		
1987	GB	Ciproxin	Bayer		
1989	IT	Ciproxin	Bayer		
1989	IT	Flociprin	IBI		
	IT	Oftacilox	Alcon		
	JP	Ciproxan	Bayer		
	US	Ciloxan	Alcon		
1987	US	Cipro	Bayer		

FRM amp. 100 mg/10 ml, 200 mg/200 ml, 400 mg/400 ml; eye drops 3 mg/3 ml; gran. 20%; tabl. 100 mg, 200 mg, 250 mg, 500 mg, 750 mg; vial 100 mg/50 ml, 200 mg/100 ml, 300 mg/150 ml (as hydrochloride)

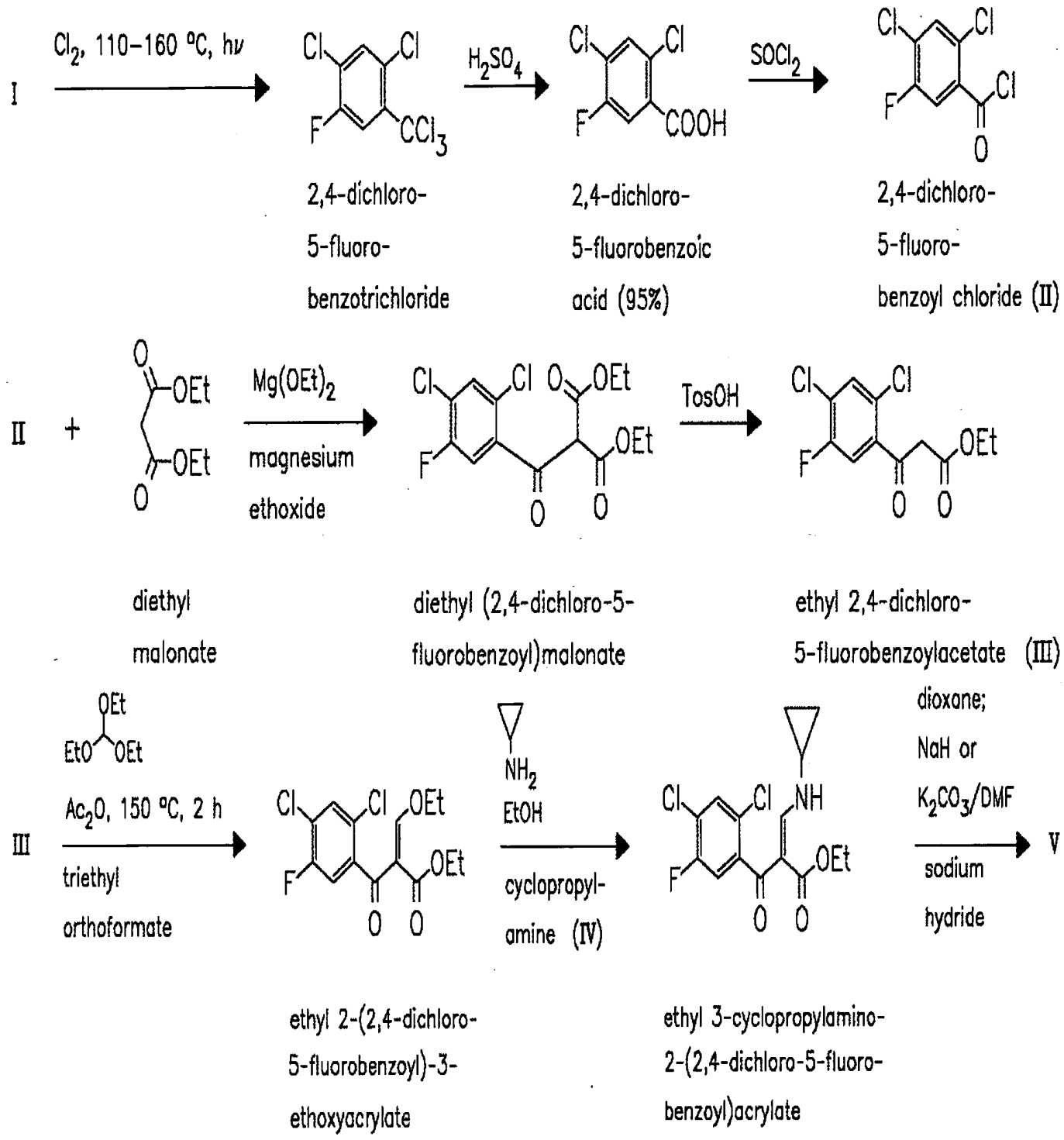
PRE

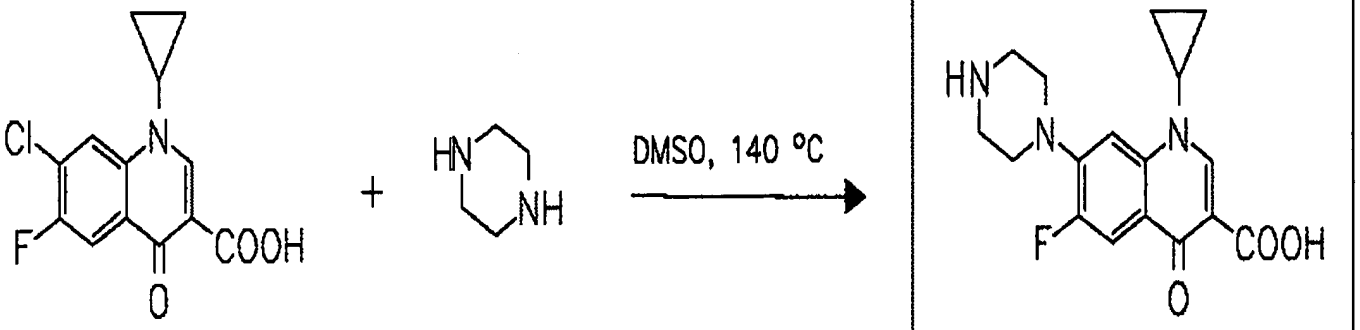
(a)



2,4-dichloro-5-methylaniline

(I)


I
Cl2, 110–160 °C, hν
H2SO4
SOCl2
2,4-dichloro-5-fluoro-benzotrichloride
2,4-dichloro-5-fluorobenzoic acid (95%)
2,4-dichloro-5-fluoro-benzoyl chloride (II)
II
+
Mg(OEt)2
magnesium ethoxide
TosOH
diethyl malonate
diethyl (2,4-dichloro-5-fluorobenzoyl)malonate
ethyl 2,4-dichloro-5-fluorobenzoylacetate (III)
III
Ac2O, 150 °C, 2 h
triethyl orthoformate
NH2
EtOH
cyclopropyl-amine (IV)
dioxane; NaH or K2CO3/DMF
sodium hydride
V
ethyl 2-(2,4-dichloro-5-fluorobenzoyl)-3-ethoxyacrylate
ethyl 3-cyclopropylamino-2-(2,4-dichloro-5-fluoro-benzoyl)acrylate

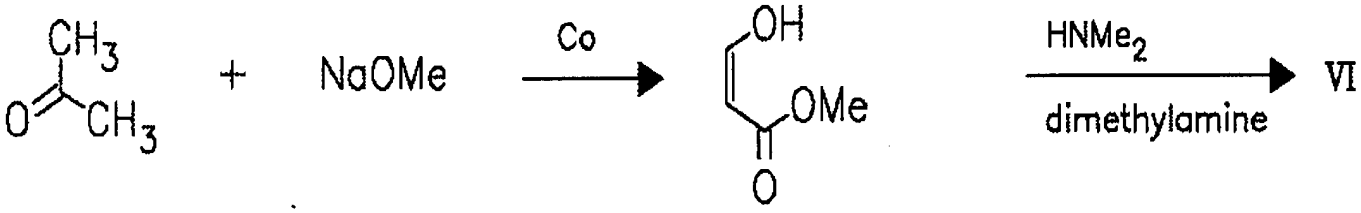


7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid (V)

piperazine

Ciprofloxacin

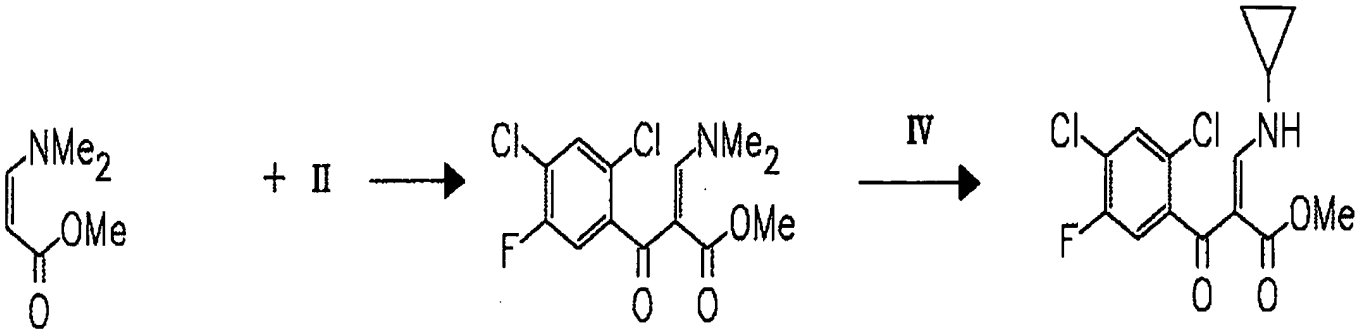
(b)



acetone

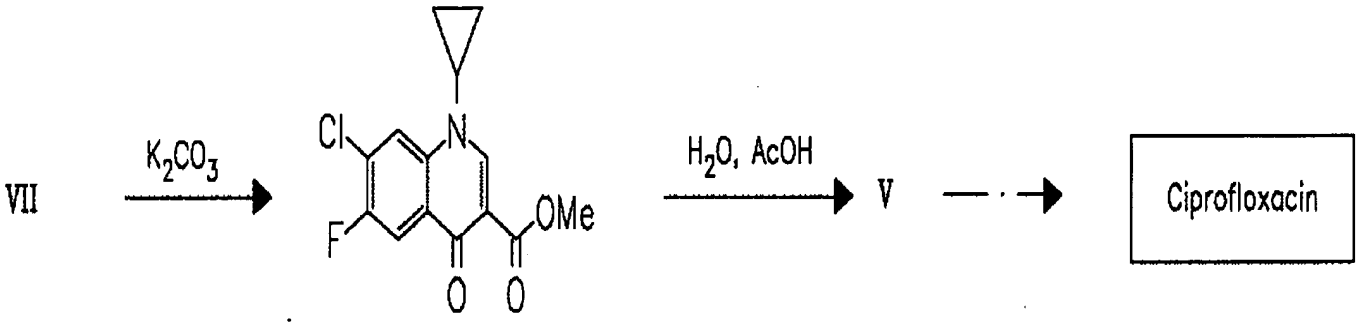
sodium methylate

methyl 3-hydroxyacrylate



methyl 3-dimethylamino-acrylate (VI)

(VII)



INT

RN.INT	MF.INT	CN.INT
67-64-1	C3H6O	acetone; 2-Propanone
86393-33-1	C13H9ClFNO3	7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid; 3-Quinolinecarboxylic acid, 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-
104599-90-8	C14H11ClFNO3	7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid methyl ester; 3-Quinolinecarboxylic acid, 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-, methyl ester
765-30-0	C3H7N	cyclopropylamine; Cyclopropanamine
105392-26-5	C14H12Cl2FNO3	2,4-dichloro-α-[(cyclopropylamino)methylene]-5-fluoro-β-oxobenzenepropanoic acid methyl ester; Benzenepropanoic acid, 2,4-dichloro-α-[(cyclopropylamino)methylene]-5-fluoro-β-oxo-, methyl ester
105392-19-6	C13H12Cl2FNO3	2,4-dichloro-α-[(dimethylamino)methylene]-5-fluoro-β-oxobenzenepropanoic acid methyl

		ester; Benzenepropanoic acid, 2,4-dichloro-α-[(dimethylamino)methylene]-5-fluoro-β-oxo-, methyl ester
86522-89-6	C7H3Cl2FO2	2,4-dichloro-5-fluorobenzoic acid
86522-88-5	C7H2Cl5F	2,4-dichloro-5-fluorobenzotrichloride
86393-34-2	C7H2Cl3FO	2,4-dichloro-5-fluorobenzoyl chloride; Benzoyl chloride, 2,4-dichloro-5-fluoro-
86522-86-3	C7H5Cl2F	1,5-dichloro-2-fluoro-4-methylbenzene
17601-75-1	C7H7Cl2N	2,4-dichloro-5-methylaniline
86522-85-2	C9H11Cl2N3	1-(2,4-dichloro-5-methylphenyl)-3,3-dimethyl-1-triazene
86483-50-3	C14H13Cl2FO5	diethyl (2,4-dichloro-5-fluorobenzoyl)malonate; Propanedioic acid, (2,4-dichloro-5-fluorobenzoyl)-, diethyl ester
105-53-3	C7H12O4	diethyl malonate; Propanedioic acid, diethyl ester
124-40-3	C2H7N	dimethylamine; Methanamine, N-methyl-
86483-53-6	C15H14Cl2FNO3	ethyl 3-cyclopropylamino-2-(2,4-dichloro-5-fluorobenzoyl)acrylate; Benzenepropanoic acid, 2,4-dichloro-α-[(cyclopropylamino)methylene]-5-fluoro-β-oxo-, ethyl ester
86483-51-4	C11H9Cl2FO3	ethyl 2,4-dichloro-5-fluorobenzoylacetate; Benzenepropanoic acid, 2,4-dichloro-5-fluoro-β-oxo-, ethyl ester
86483-52-5	C14H13Cl2FO4	ethyl 2-(2,4-dichloro-5-fluorobenzoyl)-3-ethoxyacrylate; Benzenepropanoic acid, 2,4-dichloro-α-(ethoxymethylene)-5-fluoro-β-oxo-, ethyl ester
122-51-0	C7H16O3	ethyl orthoformate; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-
999-59-7	C6H11NO2	methyl 3-dimethylaminoacrylate; 2-Propenoic acid, 3-(dimethylamino)-, methyl ester
86761-97-9	C4H6O3	methyl 3-hydroxyacrylate; 2-Propenoic acid, 3-hydroxy-, methyl ester
122-51-0	C7H16O3	orthoformic acid triethyl ester; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-
110-85-0	C4H10N2	piperazine; Piperazine
124-41-4	CH3NaO	sodium methylate; Methanol, sodium salt
122-51-0	C7H16O3	triethoxymethane; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-
122-51-0	C7H16O3	triethyl orthoformate; Ethane, 1,1',1''-[methylidynetris(oxy)]tris-

RE

(1) EP 49 355 (Bayer AG; appl. 21.8.1981; D-prior. 3.9.1980).
(2) US 4 670 444 (Bayer AG; 2.6.1987; D-prior. 3.9.1980).
(3) DE 2 808 070 (Bayer; 24.2.1978)
(4) DE 3 273 892
(5) DE 3 502 935 (Bayer; 29.9.1984)
(6) DOS 3 142 854 (Bayer AG; appl. 29.10.1981).
(7) US 4 620 007 (Bayer AG; 28.10.1986; D-prior. 3.9.1980, 29.10.1981).
(8) Grohe, K.; Heitzer, H.: Liebigs Ann. Chem. (LACHDL) 1987, 29.

one-pot production:

(9) EP 657 448 (Bayer AG; appl. 28.11.1994; D-prior. 10.12.1993).
alternative synthesis:
(10) EP 657 448 (Bayer; 28.11.1994; D-prior. 10.12.1993)
ciprofloxacin hydrate preparation:
(11) WO 200 185 692 (Natco Pharma; 19.3.2001; IN-prior. 9.5.2000)
storage stable infusion solution:
(12) DE 19 930 557 (Bayer; 2.7.1999)
new formulation:
(13) WO 200 226 233 (Fresenius; appl. 27.9.2001; D-prior. 29.9.2000)
topical aqueous formulation:
(14) US 5 286 754 (Bayer; 15.2.1994; appl. 19.9.1988; D-prior. 21.1.1986)
controlled release tablet/oral formulation:
(15) US 2 002 037 884 (Alcon; 28.3.2002; USA-prior. 26.7.2000)
(16) WO 200 164 183 (Ranbaxy; appl. 28.10.2001; USA-prior. 3.3.2000)
aqueous infusion solution:
(17) US 6 261 601 (Ranbaxy; 17.7.2001; IN-prior. 19.9.1997)
composition with improved solubility and decreased irritation in opthalmic use:
(18) DE 19 730 023 (Bayer; 11.7.1997)
(19) WO 9 637 191 (Alcon; 24.5.1995)

START LOCAL KERMIT RECEIVE PROCESS

BINARY DATA HAS BEEN DOWNLOADED TO MULTIPLE FILES 'IMAGEnnn.TIF'

=> d his

(FILE 'HOME' ENTERED AT 10:05:33 ON 19 DEC 2006)

FILE 'CASREACT, CHEMINFORMRX, DJSMONLINE, PS' ENTERED AT 10:05:55 ON 19 DEC 2006

L1 STRUCTURE UPLOADED
L2 11 S L1
L3 104 S L1
L4 283 S L3 AND POTASSIUM PHOSPHATE TRIBASIC OR (K3PO4)
L5 1 S L3 AND((POTASSIUM PHOSPHATE TRIBASIC) OR (K3PO4))
L6 0 S L3 AND (ORGANIC SOLVENT)
L7 103 S L3 NOT L5

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 10:14:41 ON 19 DEC 2006

Connecting via Winsock to STN

W* * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

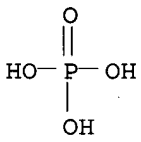
FILE 'HOME' ENTERED AT 10:31:38 ON 19 DEC 2006

=> file reg

=> s k3po4
L5 1 K3PO4

=> d

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 7778-53-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN Phosphoric acid, tripotassium salt (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Potassium orthophosphate
CN Potassium phosphate
CN Potassium phosphate (K3PO4)
CN Potassium tribasic phosphate
CN Tripotassium orthophosphate
CN Tripotassium phosphate
DR 44042-47-9
MF H3 O4 P . 3 K
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGU, GMELIN*, IFICDB, IFIPAT, IFIUDB, MRCK*, MSDS-OHS, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (7664-38-2)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2378 REFERENCES IN FILE CA (1907 TO DATE)
15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2382 REFERENCES IN FILE CAPLUS (1907 TO DATE)

8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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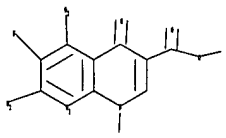
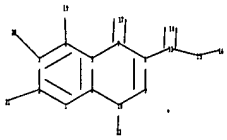




chain nodes :
13 14 15 16 17 19 20 21
ring nodes :
1 2 3 4 5 6 7 8 9 10
ring/chain nodes :
22
chain bonds :
2-21 3-20 4-19 7-17 8-13 10-22 13-14 13-15 15-16
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
exact/norm bonds :
1-2 1-6 2-3 2-21 3-4 3-20 4-5 4-19 5-6 5-7 6-10 7-8 7-17 8-9 8-13
9-10 10-22 13-14 13-15 15-16

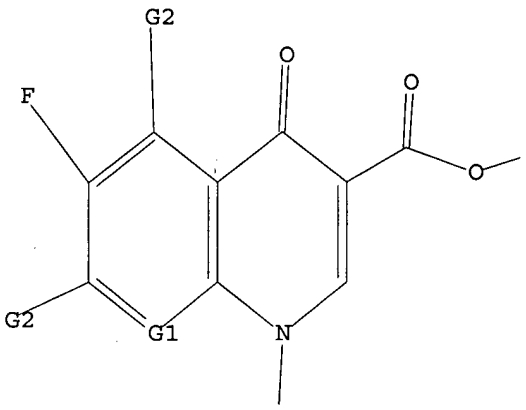
G1:C,N

G2:H,X

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 19:CLASS 20:CLASS 21:CLASS
22:CLASS

L6 STRUCTURE UPLOADED

=> d l6
L6 HAS NO ANSWERS
L6 STR



G1 C,N

G2 H,X

Structure attributes must be viewed using STN Express query preparation.

=> s l6 full
L7 917 SEA SSS FUL L6

=> file ca
C

=> s l7
L8 624 L7

=> s l5
L9 2378 L5

=> s l8 and l9
L10 1 L8 AND L9

=> d ibib abs hitstr

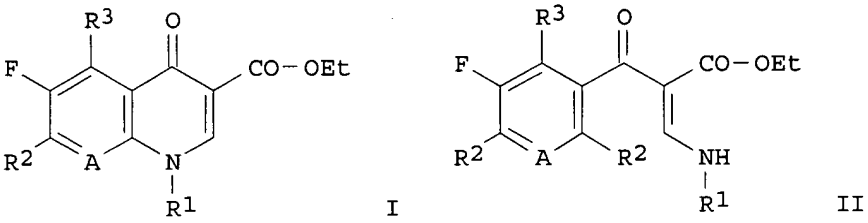
L10 ANSWER 1 OF 1 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 141:89022 CA
TITLE: Preparation of quinolonecarboxylate derivatives
INVENTOR(S): Lee, Tai-Au; Park, Nam-Jin; Khoo, Ja-Heouk; Song, Seong-Ho; An, Ju-Young
PATENT ASSIGNEE(S): Yuhan Corporation, S. Korea
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056781	A1	20040708	WO 2003-KR2785	20031219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2004055527	A	20040626	KR 2002-82222	20021221
CA 2508341	A1	20040708	CA 2003-2508341	20031219
AU 2003286968	A1	20040714	AU 2003-286968	20031219
EP 1572657	A1	20050914	EP 2003-777472	20031219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006514033	T	20060427	JP 2004-562091	20031219
US 2006058528	A1	20060316	US 2005-537945	20050609

PRIORITY APPLN. INFO.: KR 2002-82222 A 20021221
WO 2003-KR2785 W 20031219

OTHER SOURCE(S): CASREACT 141:89022; MARPAT 141:89022
GI



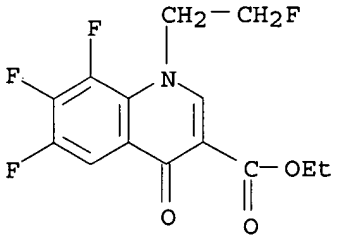
I II

AB Title compds. I [R1 = cyclopropyl, 2,4-difluorophenyl, 1-acetoxy-2(S)-yl; R2, R3 = H, Cl, F; A = CH, CF, CNO2, N] are prepared by reaction of aminoacrylates II with K3PO4 in organic solvent. Thus, reaction of Et 3-cyclopropylamino-2-(pentafluorobenzoyl)acrylate in MeCN in the presence of K3PO4 at 75-80° for 1.5 h gave 96.9% Et 1-cyclopropyl-5,6,7,8-tetrfluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate.

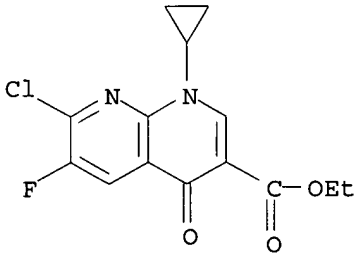
IT 93969-13-2P 96568-07-9P 98349-25-8P
100491-29-0P 107564-02-3P 108138-17-6P
289688-78-4P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of quinolonecarboxylate derivs.)

RN 93969-13-2 CA

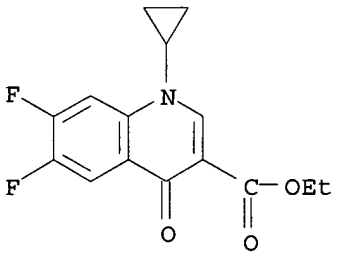
CN 3-Quinolinecarboxylic acid, 6,7,8-trifluoro-1-(2-fluoroethyl)-1,4-dihydro-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



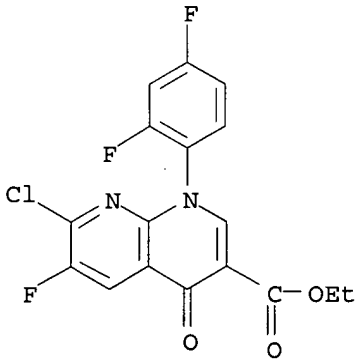
RN 96568-07-9 CA
CN 1,8-Naphthyridine-3-carboxylic acid, 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



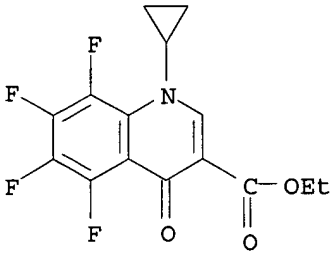
RN 98349-25-8 CA
CN 3-Quinolinecarboxylic acid, 1-cyclopropyl-6,7-difluoro-1,4-dihydro-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



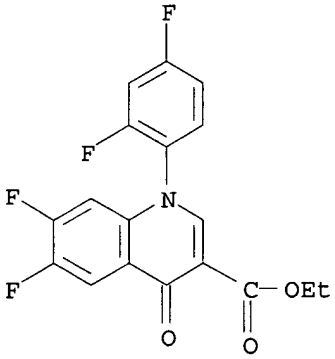
RN 100491-29-0 CA
CN 1,8-Naphthyridine-3-carboxylic acid, 7-chloro-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 107564-02-3 CA
CN 3-Quinolinecarboxylic acid, 1-cyclopropyl-5,6,7,8-tetrafluoro-1,4-dihydro-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)

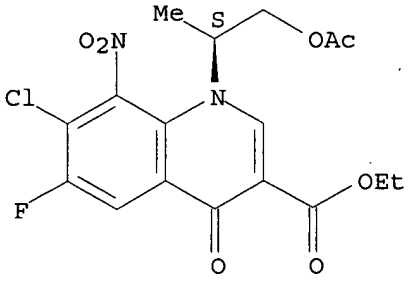


RN 108138-17-6 CA
CN 3-Quinolinecarboxylic acid, 1-(2,4-difluorophenyl)-6,7-difluoro-1,4-dihydro-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)

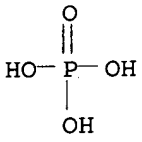


RN 289688-78-4 CA
CN 3-Quinolinecarboxylic acid, 1-[(1S)-2-(acetyloxy)-1-methylethyl]-7-chloro-6-fluoro-1,4-dihydro-8-nitro-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 7778-53-2, Potassium phosphate
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of quinolonecarboxylate derivs.)
RN 7778-53-2 CA
CN Phosphoric acid, tripotassium salt (8CI, 9CI) (CA INDEX NAME)



●3 K

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 10:34:36 ON 19 DEC 2006